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CONTENTS OF PREVIOUS NUMBER

FEBRUARY, 1931. NUMBER 2

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VOLUME 25 MARCH, 1931 NUMBER 3

CEREBRAL BIRTH CONDITIONS, WITH SPECIAL REFERENCE TO CEREBRAL DIPLEGIA

A PRELIMINARY REPORT OF A CLINICAL STUDY *

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The problem of the neurologic conditions which are found at birth or which give evidence of their presence within a variable time after birth has been the subject of much discussion for many years. The varied names applied to these conditions and the numerous types of pathologic changes which have been reported are evidence of the confusion which exists. Obstetricians, pediatricians, pathologists and neurologists have contributed something from the special points of view of their particular work, but there has been no common agreement among them as to etiology.

For the most part the main issue raised by all groups has been the part played by birth injuries in the production of neurologic states, and it is to some particular phases of this problem that my attention has been directed.

The questions to be answered are, in the main, whether one must consider fetal disease *sui generis,* developmental defects, disorders of growth, maternal diseases and conditions, hereditary influences, or traumatizations of the nervous system the basic factors in the neurologic conditions of the new-born infant.

CASE MATERIAL

For the purpose of this study a group of forty-six cases have been analyzed. In order to consider the part that is possibly played by birth trauma, the patients have been separated into two groups, the first comprising those in which there is a definite history of difficult labor and the second those in which labor was considered in every respect normal. At the start, however, difficulties have arisen, as no one, not even he who is most intimately concerned with the problem—the obstetrician—has been able to define normal labor. For the present purpose, nevertheless, it seems permissible to employ the term "normal labor," and by that I mean one which was not prolonged, in which the presentation was usual and no anesthetics or instruments were used

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and in which birth was not precipitate or difficult and the delivery could, in all respects, be considered spontaneous. The term "difficult labor" implies the exact opposite to spontaneous, normal delivery and includes cesarean section.

As the large majority of my cases presented a disorder of the motor apparatus, the so-called cerebral infantile paralyses are singled out for special consideration. Because of the lack of extensive research and complete histopathologic facts, the subject of cerebral infantile paralysis offers no opportunity for dogmatism, but does lend itself perhaps to some generalization from the clinical standpoint and some

TABLE 1.—*Composite Summary of Case Histories Showing the Distribution of Symptoms in the Two Groups*

Symptoms	Group 1—Difficult Labor	Group 2—Normal Labor
Age at time of examination	7 months to 16 years	19 months to 12 years
Sex distribution	9 male, 10 female	14 male, 13 female
Length of term	Full, 15 cases; uncertain, 4 cases	Full, 21 cases; premature, 5 cases; uncertain, 1 case
Ages sat alone	Never, 5 cases; 8 months to 2 years, 5 cases; uncertain, 9 cases	Never, 7 cases; less than 1 year to 2 years, 6 cases; uncertain, 14 cases
Ages walked alone	Never, 6 cases; 1 to 4 years, 9 cases; uncertain, 4 cases	Never, 11 cases; 1 to 7 years, 12 cases; uncertain, 4 cases
Ages talked	Never, 4 cases; 8 to 12 months, 14 cases; unintelligibly, 1 case	Never, 8 cases; 7 months 4 years, 9 cases; not known, 6 cases; few words, 2 cases; unintelligibly, 2 cases
First symptoms noted	At birth, 6 cases; up to 6 months, 0 cases; 7 to 12 months, 1 case; 13 to 18 months or uncertain, 12 cases	At birth, 5 cases; up to 6 months, 3 cases; 7 to 12 months, 5 cases; 13 to 18 months, 3 cases; 18 months or uncertain, 11 cases
Spasticity	Bilateral, 7 cases; none, 7 cases; unilateral, 4 cases; bilateral Babinski, no spasticity, 1 case	Bilateral, 15 cases; none, 3 cases; unilateral, 3 cases; bilateral Babinski, no spasticity, 6 cases
Abnormal movements: athetoid, choreiform, incoordinate, etc.	Absent, 10 cases; present, 9 cases	Absent, 14 cases; present, 13 cases
Convulsions	6 cases	3 cases
Intelligence	Normal, 6 cases; defective, 11 cases; uncertain, 2 cases	Normal, 1 case; defective, 26 cases

theorizing from the phylogenetic, embryologic and developmental points of view.

Since this is a group study, the individual case records are not given, but instead a composite summary of the two groups is given. Of the forty-six cases, nineteen fall into the difficult labor group and twenty-seven into the "normal" group.

On analyzing table 1, it is readily seen that the sexes are about equally divided, so that there is perhaps no question regarding the increased size of the head in the male as a causative factor. The length of term was less than nine months in the normal group in five cases, but they were included in this group because labor was not difficult and because the symptoms presented were in no way different from those in the full term cases. Unfortunately, the histories did not

mention the order of birth in all cases, and therefore the influence of parity could not be ascertained.

Children in the difficult labor group never sat alone in 26 per cent of the cases, and in the "normal" group in 25 per cent; never walked alone in 31 per cent of the "abnormal" cases as compared to 40 per cent in the "normal" group; 21 per cent of the difficult labor group never talked as compared with 29 per cent of the "normal" labor group.

It is of interest that frank evidence of motor disability was not observed in the majority of instances in both groups until some time after birth. The usual history given is that these children were not considered abnormal until the time came when ordinarily they should be carrying out some of the motor functions of their age period. Not infrequently they were brought to the physician with the complaint

TABLE 2.—*Distribution of Symptoms in the Two Groups Expressed in Percentages*

	Difficult Labor, per Cent	Normal Labor, per Cent
Sexes	Equally divided	Equally divided
Never sat alone	26.0	25.0
Never walked alone	31.0	40.0
Never talked	21.0	29.0
Bilateral pyramidal involvement	42.1	77.7
Hemiplegia	21.0	11.1
No pyramidal involvement	36.8	11.1
Abnormal movement	47.0	48.0
Convulsions	30.0	10.0
Mentally defective	68.0	96.0

from the parents that they did not sit up, could not walk or had never talked.

The most interesting feature of the group taken as a whole was evidence of involvement of the pyramidal tract in a group in which labor was considered normal. The incidence of unilateral spasticity was greater in the difficult labor group, 21 per cent, as compared with 11.1 per cent in the "normal" group, a proportion of almost 2:1. The remaining cases also offer an interesting and striking contrast, for the difficult labor group had 35.8 per cent with no evidence of involvement of the pyramidal tract as compared to 11.1 per cent in the "normal" labor group, an incidence of more than 3:1.

The occurrence of abnormal movement was not as great as many authors would lead one to expect. By abnormal movement I am referring to choreiform and athetoid movements and definite incoordinations that arise as a result of disturbance in the striatal and other related systems. Nearly one half of the total number showed abnormal movement in both groups, 47 per cent in the "difficult" and 48 per cent in the "normal" group.

Convulsions were likewise not as frequent as one might have expected; they occurred in 30 per cent of the difficult labor group as compared with about 10 per cent in the "normal" labor group.

The estimation of intelligence in many cases was difficult. In at least one half of the entire group a psychometric examination was made, but in the remainder an approximate rating only was possible. Allowing for a certain percentage of error, however, the two groups afford a striking contrast. In the "normal" labor group intelligence was considered defective in all but one case; that is, in 96 per cent there was an estimated intelligence deficit. On the other hand, the "difficult" labor group had six cases in which the children were considered to be normal and thirteen, or 68 per cent, defective. As a whole, however, there is unquestionably a low level of intelligence for the entire group.

From these data I believe that it is possible to conclude that irrespective of birth history certain syndromes appear, showing practically identical symptoms. There is a disturbance of motor function more or less symmetrically distributed, giving evidence of disease or defect of the motor equipment of the individual and an accompanying low level of intelligence.

POSSIBILITIES OF DEVELOPMENT DEFECTS

Irrespective of the accepted theory of etiology, it is perhaps with some profit in the general perspective to look on the cerebral infantile palsies from the developmental point of view. On tracing the motor patterns from birth in the normal child up to the period at which he has full motor control, one finds that there is a regular progression of development and achievement. At birth, the child begins breathing and is able to perform the suctorial and deglutitional functions necessary to maintain life, but that is all. As time goes on, he moves his head from side to side; then he is able to raise his head from the bed and, finally, to hold it erect without support. Next he acquires control of the arm movements to a certain degree and can sit alone. Then he gets on his knees and crawls about in the manner of a four-legged animal. Then comes the ability to stand without aid and finally to walk. There is a variation, of course, in different children as to the rapidity with which they reach the final stage of motor control, but, be that as it may, they all pass through the same stages of a developmental process.

Coghill's[1] monograph "Anatomy and the Problem of Behaviour" supports this. He stated (1) that "the behaviour pattern develops in a regular order of sequence of movements which is consistent with the

1. Coghill, G. E.: Anatomy and the Problem of Behaviour, New York, The Macmillan Company, 1929.

order of development of the nervous system in its parts; (2) in a relatively precise manner physiological processes follow the order of their embryological development; (3) behaviour develops from the beginning through the progressive expansion of a perfectly integrated total pattern."

The careful observations made by Coghill lend much weight to his deductions. Following the dicta quoted, what is the situation in cerebral diplegia? As previously mentioned, these children are born with fully developed neuromuscular equipment for the procuring of food and satisfying the needs of life. This stage of development seems to be common to the normal and abnormal alike, but in the weeks and months following birth a marked difference between the two is noted. Cases of cerebral infantile paralysis proceed but slowly (albeit in the same "regular order of sequence of movements") and never reach a period of "progressive expansion of a perfectly integrated total pattern." A failure of complete development is manifest and, be it noted, not a retrogression to a still more helpless state. The children who survive for a score of years or less may, and probably do, show a progressive deterioration physically, but in the present state of knowledge it is impossible to state whether this deterioration is due to the congenitally poor equipment of the child or to the influence of incidental diseases and conditions.

In analyzing cases of cerebral diplegia, it is again emphasized that the children are equipped with the motor functions necessary to sustain life. From this point onward there is a varying degree of developed motor control. Some are completely spastic and remain so until they die. Some acquire the head movements and perhaps the ability to support the head, but go no further. Others are able to use their arms with some degree of purposefulness and to sit alone, but remain helpless in the control of their lower extremities. Still others acquire some control of the lower extremities and are able to get about unaided. Finally, there is a certain percentage who show very little evidence of lack of motor control, but in whom there can be persistently demonstrated a bilateral Babinski reflex. The picture presented in these cases is a failure of development at some particular point and a definite adherence to an "orderly progression," so far as it goes, from above downward.

The fact that these cases often show better development in the control of movements of the face, neck and arms than of management of the trunk or lower extremities indicates clearly that something has happened to check the completion of the motor pattern for these children. Any theory brought forward to explain such phenomena is open to challenge, it must be admitted, but some theory offered may form

the basis for extended research along these lines and would therefore possess some possible merit.

MYELINIZATION

If one accepts the work of Flechsig and others on myelinogenesis, some help may be obtained in solving this problem. Flechsig [2] stated that myelin sheath formation follows a strictly systematic fashion from the standpoint of time and repeats the phylogenesis of the entire nervous system in accordance with the biogenetic principle of Haeckel.

The myelin sheath does not form at once along the entire length of a fiber, at least not in very long tracts like the pyramidal tracts which run without interruption from the cortex to the lower cord, but is pushed gradually downward from the cortex, always beginning by necessity at the ganglion cell or neuroblast. Flechsig stated further that he determined the lapse of time between the formation of neurits and the appearance of the myelin sheaths in the form of a closed tube as four months. He also indicated, and I hold this to be significant, the possibility of myelinization occurring simultaneously in the parts that are functionally related. According to his research, the first motor cranial nerve to be myelinated is the hypoglossus, and the first association tract the posterior longitudinal bundles, which he believed contains the centers for control of respiratory function. He assumed that the motor cranial nerves, and particularly those concerned with the functions necessary to sustain life, are all myelinated at birth, and that the motor and sensory roots of the spinal cord are also at this time fully equipped. This would mean functionally that the child could breathe, eat and move the arms and legs in a spinal reflex manner, which seems to be the case. Flechsig's theory in the latter respect is borne out in an article by d'Abundo [3] in a study of the myelinization of the spinal cord. He stated in part that at birth there exists a maturity of myelinization of the spinal cord sufficient to the immediate requirements of the life of nutrition and of the life of relation, and that this maturity takes place independently of the cerebrum.

The best practical demonstration of the relationship of myelinization to development of function is the careful work of Tilney and Casamajor,[4] which supports in a large way Flechsig's theory. They studied the behavior of kittens from birth to the age of complete motor control and correlated their clinical observations with the development of

2. Flechsig, P.: Meine myelogenetische Hirnlehre mit biographischer Einleitung, Berlin, Julius Springer, 1927.

3. d'Abundo, E.: Some Peculiarities in the Development and in the Myelinization of the Spinal Cord, Riv. ital. di neuropat. **14**:65, 1921.

4. Tilney, F., and Casamajor, L.: Myelinogeny as Applied to the Study of Behavior, Arch. Neurol. & Psychiat. **12**:1 (July) 1924.

myelinization by histologic examinations for each pattern development period. In part their conclusions are as follows: "Myelogeny in connection with behavioral components afford strong evidence in the cat that the deposition of myelin is coincidental with the establishment of function in definite fiber systems."

According to Wlassak,[5] myelin is first demonstrable in the embryogenic central nervous system in the protoplasm of the spongioblasts. It is of exogenous origin and brought to the central nervous system through the agency of the blood. He stated that definite fiber groups receive their myelin according to a definite chronologic schedule.

Cornwall,[6] in a study of the origin of myelin in rats, concluded that it was deposited around the axis cylinder after the axis cylinder had been formed, and that during this process there was a marked increase of vascularity. Preceding myelinization, cells were found in the ventricles and subarachnoid spaces that took the myelin stain. Similar staining cells were found in the blood vessels and later within the axis at the level of the lateral processes of the fourth ventricle. He also found structures having the appearance of hollow tubes in the axis before myelin appeared, the staining reactions of which would indicate that they contain fatty acid. His work would seem to indicate a dependence in myelogenesis on proper vascularization under normal conditions. What then might be the fate of the axis cylinders, so far as the myelin sheath is concerned, if there is an alteration in the blood itself, with deficit of the myelin-forming substances? And can these observations on the rat be applied to the human being?

Hirako's[7] report also lends some support to the part played by the blood stream in myelinization; he stated, in agreement with Monakow, that he believed that the fibers best supplied with blood vessels show the earliest myelinization. It is also apparent that the phylogenetically older portions of the brain, such as the hippocampus and the uncus, show an earlier myelinization than the rest.

A possible theory would be that interference with myelinization might come about in fetal life through alteration of the blood from toxic or infectious conditions in the mother and in postnatal life through improper food. It is noteworthy that the children who later show diplegia are not infrequently considered difficult feeding problems by the pediatricians, but it is not certain whether this is a cause or an effect.

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5. Wlassak, R.: Die Herkunft des Myelins, Beitr. z. Physiol. d. Nerv. **6**: 453, 1898.

6. Cornwall, L. H.: The Origin of Myelin, Arch. Neurol. & Psychiat. **18**:2 (Aug.) 1927.

7. Hirako, G.: Concerning Myelinization in the Cerebral Cortex, Schweiz. Arch. f. Neurol. u. Psychiat **10**:275, 1922.

The well known clinical and histologic picture of multiple sclerosis illustrates the departure of function with loss of the myelin sheaths leaving the axis cylinders naked. There then develop spasticity and alteration of muscle tone and movement.

The mention of an adult nervous disease of a degenerative type brings up another rather striking parallelism from the standpoint of motor developmental defect, which may have some connection with the problem at hand. I am referring to the chronic heredodegenerative group which Orton [8] reported from the pathologic standpoint, stating: "One interesting fact coming out of a review of the hereditary and familial nervous diseases is the great predominance in the motor field."

It seems possible to assume, then, that in cerebral diplegia, and possibly many other conditions, myelogenesis ceases at some particular period in intra-uterine or postnatal life. But from what cause?

BIRTH INJURY THROUGH HEMORRHAGE AND TRAUMATIZATION OF THE MENINGES AND CEREBRAL TISSUE

The possible factor of birth injury producing various types of intracranial lesions has been widely discussed. For the most part some particular phase of the problem has been emphasized, and complete studies of the entire brain have usually not been made. Hemorrhage has been prominently mentioned as an etiologic factor by the majority of authors, following the lead of Dr. Sarah McNutt.[9] On the basis of a history of difficult labor and choked disks, subtemporal decompression was frequently performed for the relief of intracranial hemorrhage by Sharpe and Farrell.[10] They studied sixty-five cases and found that thirty-four were diplegias, eleven paraplegias and twenty hemiplegias. The usual pathologic changes were supracortical fibrous or cystic formations, supposedly the result of birth hemorrhages.

In 300 cases coming to necropsy, Schwartz [11] reported hemorrhage and softening in 65 per cent. He reported Saenger as finding severe intracranial hemorrhages in 64 and slight hemorrhages in 27 of 100 cases. In an editorial appearing in *The Journal of the American*

8. Orton, S. T.: The Pathology of the Hereditary and Familial Nervous and Mental Diseases, Arch. Neurol. & Psychiat. **13**:96 (Jan.) 1925.

9. McNutt, Sarah: Double Infantile Spastic Hemiplegia with Report of Case, Am. J. M. Sc. **89**:78, 1885.

10. Sharpe, W., and Farrell, B. P.: The Treatment of Cerebral Spastic Paralysis by Subtemporal Decompression, J. A. M. A. **64**:482 (Feb. 6) 1915.

11. Schwartz, P.: Traumatic Injury of the Brain at Birth and Pathology of Earliest Childhood, Deutsche med. Wchnschr. **50**:1375, 1924.

Medical Association,[12] Ehrenfest[13] is quoted as remarking that obstetricians have succeeded in revealing the exact mechanism in the origin of most of the more common types of cranial and intracranial lesions sustained by the child in the course of birth. Pediatricians have also made valuable contributions, chiefly in regard to the symptomatology. "They have discovered the evident etiologic relation of intracephalic birth hemorrhages to a reduced coagulability of the blood, rather frequently ascertainable in the new born."

There seems to be a widespread impression that the causation of intracranial birth hemorrhages often involves factors having no direct relation to labor, and the "explanations may be summarized under the vague designation of hemorrhagic disease beginning in intra-uterine life." Ehrenfest believed that undue stress has been laid on the hemorrhagic diathesis, and that the widespread significance of both artificial mechanical and physiologic trauma incident to birth has been overlooked. Palmer[14] investigated the causes of death in children born dead or dying shortly after birth. There were 144 cases with 39 macerated fetuses. Ninety-one of the 99 stillborn showed evidences of death by asphyxia, and in 7 cases there was hemorrhage into the dura, though not extensive enough to cause death. In 12 cases in which asphyxia was determined, death was due apparently to intracranial hemorrhage consequent to excessive molding of the head. The conclusions regarding the 99 cases of stillbirth are that maternal diseases caused 26 deaths, fetal disease 3 and labor 70. There is no record in this report, however, of histologic examinations.

Cornwall[15] enumerated the ascribed causes of infantile palsies, including among others leptomeningeal hemorrhage, intracerebral hemorrhage, subdural hemorrhage and sinus thrombosis. He believed that intracranial hemorrhage when bilateral will produce diplegia, and that subdural hemorrhages are the most important, especially when they originate in the vicinity of the tentorium cerebelli. Here both blades of the free edge may be torn, but he stated that the large extravasations of blood into the brain substance are limited for the most part to the soft brains of premature infants. Moreno[16] performed necropsies on

12. Intracranial Birth Hemorrhages, Editorial, J. A. M. A. **82**:395 (Feb. 2) 1924.

13. Ehrenfest, H.: The Causation of Intracranial Hemorrhage in the New-Born, Am. J. Dis. Child. **26**:503 (Dec.) 1923.

14. Palmer, A. C.: The Cause of Fetal Death in 144 Cases, Medical Research Council, Special Rep. ser. no. 118, Child Life Investigations, London, His Majesty's Stationery Office, 1928.

15. Cornwall, L. H.: Neurologic Aspects of Injuries at Birth, Arch. Neurol. & Psychiat. **20**:430 (Aug.) 1928.

16. Moreno, S. F. M.: The Effect of Trauma on the Neurological Disorders in Children, Arch. mens. d'obst. et de gynéc. **4**:145, 1915.

forty new-born children and found laceration of the tentorium in ten and rupture of the falx cerebri in five. Experimental work on cadavers proved that similar lesions could be caused by exerting pressure on the sides of the head.

PORENCEPHALY AND ENCEPHALITIS

Globus [17] reviewed the literature on this subject and quoted Heschl, who in 1859 introduced the term to designate a defect in the brain characterized by cavity formation due to faulty development during intra-uterine life or to regressive destructive processes caused by occlusion of the vessel. Globus summarized Kundrat's views, published in 1882, somewhat as follows: 1. Most of the porencephalic defects are congenital although infrequently they may be acquired later. 2. Hemorrhage, thrombosis, embolism, violent intra-uterine contractions, hydrocephalus, anemia and psychic disturbances occurring to the mother during pregnancy may cause porencephalic defects. 3. Porencephalic loss may be so pronounced that life is early terminated, but the patient might mature with a definite mental defect. 4. Destruction or atrophy of a hemisphere may be compensated for by relative hypertrophy of the opposite hemisphere.

Schultze [18] suggested an infectious encephalitis as a cause for porencephaly, having found evidences of inflammatory changes microscopically, and he believed that the changes began in intra-uterine life. Virchow [19] established the existence of congenital encephalitis as the result of infection in the mother and stated: "It is most probable that many cases of idiopathic and deuteropathic paralyses of the infant and many instances of idiocy can be traced back to such encephalitic changes."

Strümpell [20] studied encephalitis in children clinically and anatomically and concluded that many porencephalic defects were due to this cause.

Sachs and Petersen [21] came to the conclusion that porencephalus was a secondary condition. They believed that atrophy and sclerosis might

17. Globus, J. H.: A Contribution to the Histopathology of Porencephalus, Arch. Neurol. & Psychiat. **6**:652 (Dec.) 1921.

18. Schultze, F.: Beitrag zur Lehre von den angeborenen Hirndefecten (Porencephalie), 58 Versammlung, Deutscher Naturforscher und Aerzte in Strassburg, 1883.

19. Virchow, R.: Congenital Encephalitis and Myelitis, Virchows Arch. f. path. Anat. **38**:129, 1867.

20. Strümpell: Ueber die acute Encephalitis der Kinder, Jahrb. f. Kinderh. **22**: 612, 1884.

21. Sachs, B., and Petersen: Study of Cerebral Palsies of Early Life Based Upon an Analysis of One Hundred and Forty Cases, J. Nerv. & Ment. Dis. **17**: 319, 1890.

be due to a polioencephalitis, though necropsy observations did not show encephalitis.

Globus reported one case with careful anatomic and histologic observations. The child developed normally until 4 months of age. It was born at full term and by normal delivery. The first observation was that the child failed to make progress mentally and acted as though it were blind and deaf. The upper and lower extremities, when examined at the age of 11 months, showed spasticity with exaggerated reflexes. At necropsy, it was noted that the frontal and parietal areas were poorly developed and the meninges thickened, with atrophy of the parieto-occipital lobes, absence of the second and third left temporal gyri, distended ventricles and the brain nothing but a shell. Microscopically, the leptomeninges of the frontal lobes showed inflammatory changes and there was thickening of the leptomeninges in the parieto-occipital areas. The vessels were cut off by meningeal scarring, and sclerotic changes were found in the cortical and subcortical substances in areas supplied by these vessels. Globus expressed the belief that the earliest inflammatory reaction occurred where the condition now appeared chronic, and latest in the temporal and frontal lobes. The cortex showed badly damaged or absent ganglion cells. On the basis of the observations it was the author's opinion that an encephalitic process began in intrauterine life and progressed after birth. The normal physical development he explained on the basis of preservation of the basal ganglia, pons and medulla. He did not consider the process traumatic, but believed that the primary lesion was in the meninges.

Freud [22] stated that 40 per cent of all diplegias dating from birth could not be ascribed to birth conditions, and expressed the belief that any birth trauma occurring caused a cerebral laceration with subsequent monoplegia or hemiplegia.

Sachs and Hausmann [23] subscribed to porencephaly and encephalitic processes as etiologic in a certain percentage of cases of cerebral infantile paralysis. In a study of seventy-eight cases at autopsy, Sachs and Peterson [21] found two instances of porencephaly.

ATROPHY AND SCLEROSIS

The point of discussion regarding atrophy and sclerosis concerns itself mainly with the possibilities of congenital defect or the result of hemorrhagic lesions. Bielschowsky and Henneberg [24] recognized two

22. Freud, S.: Die infantile Cerebrallähmung, Vienna, Alfred Hölder, 1897.

23. Sachs, B., and Hausmann, L.: Nervous and Mental Disorders from Birth Through Adolescence, New York, Paul B. Hoeber, Inc., 1926.

24. Bielschowsky, M., and Henneberg, R.: Familial Diffuse Sclerosis (Leukodystrophia Cerebri Progressiva Hereditaria), J. f. Psychol. u. Neurol. **36**:131, 1928.

types of diffuse cerebral sclerosis—exogenous or inflammatory and endogenous or degenerative. The latter form shows a symmetrical breaking down of the myelin in the cerebral hemispheres which is replaced by a gliogenous mass that is extremely rich in fibers. This type shows a distinct family tendency and two cases are reported from the same family illustrating a "recessive motor heredity."

May [25] reported the necropsy observations in a case of left hemiplegia in childhood showing: the right hemisphere one-third smaller than the left; atrophy of the pyramidal tract, the left cerebellar hemisphere and the left half of the cord. The left hemisphere was normal.

Holt and Howland [26] called attention to the similarity between the inflammatory processes in utero and those occurring in extra-uterine life. They stated that the results of hemorrhage cannot be clearly recognized after months or years and that in certain instances the lesion is undoubtedly developmental. They recognized a cortical agenesis—a more or less complete arrest of the development of cortical cells. If the lesion is very diffuse the case is classified as diplegia, if less extensive as paraplegia, and if more or less localized as monoplegia or hemiplegia. The occurrence of diplegia and paraplegia, with the chief rigidity in the lower extremities, is four times as frequent as hemiplegia.

Hempelmann [27] and Clark [28] believed that agenetic injury at or before birth and developmental defects are responsible for cerebral infantile paralyses. Patane gave a detailed study of a microcephalic idiot, aged 19, with spastic tetraplegia, typical contractures and epilepsy. The observations at autopsy were porencephaly, microcephaly, simple hypertrophy, hydrocephalus (ex vacuo), atrophy of the corpus callosum and hypoplasia of the pyramidal tracts.

Cornwall [15] would separate the injuries occurring at birth from the developmental (prenatal) defects, but also would emphasize the possibilities in encephalitic (intra-uterine) processes.

Many authors have considered the atrophies due to vascular lesions and an anemic necrosis with cyst formation. Collier [29] held to the theory that primary neuronic degeneration was the essential lesion, with atrophic sclerosis a natural consequence. Osler reviewed all cases with

25. May, W. P.: Microgyria and Its Effects on Other Parts of the Central Nervous System, Brain **43**:26 (May) 1920.

26. Holt and Howland: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1926.

27. Hempelmann, T. C.: Cerebro-Cerebellar Diplegia, Arch. Pediat. **39**:411, 1922.

28. Clark, L. P.: Infantile Cerebro-Cerebellar Diplegia, Arch. Pediat. **30**:252, 1912.

29. Collier, J.: The Pathogenesis of Cerebral Diplegia, Brain **47**:1 (Feb.) 1924.

autopsies in 1889 and reported seven instances of convolutional atrophy and five instances of cortical sclerosis. Sachs and Hausmann [28] accepted defective development of the pyramidal tracts and cortical agenesis as definite causes of cerebral palsy.

THE PREDOMINANCE OF MOTOR INVOLVEMENT

Phylogenetically, one cannot untangle the functions belonging to the old and new motor systems, for without question intricate relationships, interdependencies and probably usurpations of function have been built up as the needs of the race have increased. Considering the subject from the standpoint of the motor levels—the spinal, suprasegmental and cortical—one finds that the suprasegmental is probably partially myelinated and the third level not at all. The functions of these three levels are definitely pyramided, the crowning achievement occurring when the cortical level has reached maturity. Looking at the problem in reverse order, phylogenetically, difficulties are immediately evident. If, for instance, the corticospinal system is completely removed, instead of a coordinated function remaining at the second motor level and the spinal level being intact, everything is thrown into confusion, so to speak. The individual is completely rigid in spasticity and helpless. Experimentation on lower animals shows that decortication does not produce loss of the standing and righting reflexes, nor does it destroy the motor functions of running, walking, etc., so long as certain mesencephalic structures are left unharmed. In man, the picture would be totally different under similar conditions, and the only interpretation that one can put on it is that the pyramidal system has acquired functions perhaps that originally belonged to the old motor system, and alterations may have occurred in what might otherwise be considered pure old motor system functions. It is my belief that a certain fusion of developmental characteristics has occurred in the old and new and that pure syndromes of one or the other cannot exist.

It cannot be denied, however, that isolated structures become diseased in some instances, and by a study of many of these some idea can be gained not only of the purpose and function of these individual structures, but also of the relationships that exist between them and others. The difficulty in the interpretation of neurologic phenomena, however, lies in the impossibility of eliminating the negative side. One thinks too little of the dynamic activity of uninvolved structures and speaks of negative conditions producing positive states. Several years ago, Dr. F. X. Dercum emphasized that destruction of the pyramidal tracts could not produce spasticity and that striatal disease cannot produce rigidity, tremor or abnormal movement.

It is therefore pertinent perhaps to think of the cerebral infantile palsies not only from the standpoint of the structures which are incapable of any function, but also from the standpoint of positive activities of undiseased structures. By and large, the group of cases under consideration demonstrates negatively a defect of the latest acquired portion of the motor system and positively an abnormal activity of the lower levels. This brings up the question of disease of the basal ganglia and convulsive disorders; but consideration of these problems is reserved for a future report.

Briefly stated, then, there are definitely known to be many prenatal conditions producing neurologic states in the new-born infant, but the question remains whether birth trauma occurring in the absence of porencephaly, tuberous sclerosis, microcephaly, hydrocephalus and the like can account for the preponderant numerical incidence of cerebral infantile paralysis. That birth trauma produces a cerebral injury cannot be denied, but whether it can cause in so many instances so striking a syndrome always with a similar pattern is open to investigation. The pressure of forceps, the overriding of bone and fractures of bones of the skull in delivery, the giving way of soft cerebral tissue from the more or less fixed and resistant bone and membranes, causing tearing of the brain substance and attached vessels, cannot be disregarded. But more important than all of these, I believe, is the stasis of cerebral circulation brought about by prolonged birth pressure, excessive molding of the head or obstruction of the cord and placental circulation, which by deprivation of nutrition produce changes in nerve cells and structures sufficient to cause definite and irreparable damage. This I think, is worthy of more than casual attention. The toxic effects of anesthetics must likewise be accepted as possible sources of cerebral damage.

But granting all these things, is it conceivable that a group of cases containing no history of difficult labor in any respect should show a percentage of 77.7 per cent of bilateral motor involvement? It is furthermore striking that the pattern of motor disorder should be so similar in the largest group of these neurologic disorders of the new-born infant—the diplegias. And still more remarkable perhaps is the fact that the large majority of all cases show, as far as one is able to determine, small evidence of involvement of sensory structures, though in many instances accurate testing is impossible for obvious reasons. They are all or nearly all diseases of the motor system of one degree or another. Furthermore, cerebral diplegia has been reported in children born by cesarean section in which there could be no question of injury to the head at birth.

In the group of cases here studied there seems to be a striking preponderance of defective development in the upper strata of the motor phylum. There is, however, more than a motor defect. Intelligence is

so generally impaired that a diffuse condition must be held accountable for the disease picture. Whether defect in myelinization is the factor or whether diffuse degeneration or defective development occurring at some period in intra-uterine or postnatal life, remains for future study. The approach to the problem would seem to be: (1) through physiologic chemistry and the careful study of the pregnant woman; (2) the further correlation of behavior patterns and myelinogenesis, and (3) careful histologic examinations of the entire nervous system in cases at different age levels.

SUMMARY

The question of the part played by birth injuries in the causation of cerebral diplegia depends on further histologic study of the entire nervous system, particularly from the standpoint of myelinogenesis. The literature on the subject contains many reports, some of them the results of careful observations checked by laboratory investigation. For the most part, however, contributions have emphasized some particular phase of the problem and stopped there. Hemorrhage or vascular disturbance of some nature seems to occupy first place, an encephalitic process of some type, second place and porencephaly third. Some vascular lesions have been considered due to intra-uterine disease, the blood vessels being thought so immature in development that they ruptured easily under the influence of pressure at birth. Fatty degeneration of the walls of the blood vessels has also been put forward as a possible locus minoris resistentiae. Actual tearing or rupturing of meningeal vessels has been noted at autopsy, and subdural or pial hemorrhage has been observed as the most frequent observation. Instances of intracerebral hemorrhage have been rare. The majority of reports would indicate that tearing of the tentorium cerebelli and less frequently of the falx is not infrequently seen at autopsy. The vessels most frequently involved are the middle cerebral arteries and veins.

Of the various encephalitic processes, localized areas attributed to an anemic necrosis or the result of some prenatal inflammatory condition are the more usual postulations. That encephalitis results from acute infectious conditions in the mother or from some of the more chronic diseases, like syphilis, seems well established.

Cortical atrophy and the so-called walnut kernel type of brain, atrophy of isolated convolutions and the like might result from many causes, but are attributed most frequently to vascular lesions.

Failure of development of certain symmetric areas without known cause has been predicated by some authors. This has been termed neuronic degeneration. Careful histologic examinations of the entire brain have been made in too few cases of diplegia from this standpoint, so that one cannot be sure that the condition is or is not a part of a generalized defect.

The gross defects in true porencephaly are well known, and, although they may produce a picture in some ways similar to cerebral diplegia, it is possible that porencephaly is only occasionally responsible for the condition. Tuberous sclerosis is not a common pathologic condition and is possibly a defect of another type.

Cysts are occasionally noted and are attributed to either hemorrhagic conditions or the results of inflammation. Microcephaly is occasionally observed in cerebral diplegia, but, on the other hand, a large number of microcephalic infants show no motor involvement and only a degree of mental defect.

Hydrocephalus occurs sometimes as a result of prenatal conditions, and the patients may be diplegic and mentally defective, but on the other hand, there are many diplegic infants and not so many cases of hydrocephalus.

CONCLUSIONS

The frequent occurrence of bilateral motor involvement together with defect in intelligence indicates something more than the effects of trauma or vascular accidents in the neurologic conditions of the newborn infant. There exists probably a developmental defect or arrest which concerns either the integrity of the cortical cells or the proper myelinization of the corticospinal tracts and association fibers.

DIFFUSE PROGRESSIVE DEGENERATION OF THE GRAY MATTER OF THE CEREBRUM *

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Knowledge of the pathology of numerous nervous disorders in infants is still in an insecure state. Save for a few diseases, little is known of the factors behind the production of organic nervous disease in infants. Every case studied from a pathologic standpoint is of interest because of the light it may throw on the neuropathology of these disorders. Consequently, the present case is reported as an addition to the knowledge of the pathology of the infantile brain.

REPORT OF CASE [1]

Clinical History.—A girl, aged 3 months, was admitted to the Hamburg Säuglingsheim in Barmbeck. The parents were apparently normal. The mother, aged 30, was said to be nervous, and the father, aged 27, was healthy. The child was the first-born, and the birth was normal in every respect. During the first few weeks, development was normal. The patient took feedings regularly, first by breast and later artificially. Before entrance to the hospital she cried a great deal, especially at night. She had attacks during which she became completely stiff. She had convulsions of the entire body, during which the face was drawn to the left.

Examination.—The child was found to be underweight. The skin was pale, but turgor was good. No intertrigo or eczema was found. The head was round, the neck short. She could creep, but was unable to hold up the head. The pupils were dilated equally and fixed. She slept a great deal and seemed hindered in her breathing. The lungs showed vesicular sounds and some dry râles at the bases. The heart was normal. The abdomen was soft. The liver was barely palpable; the spleen was normal. The patellar reflexes were active; the Babinski sign was negative. The child gave the impression of not being bright.

The spinal fluid showed nothing abnormal. The Wassermann reactions of the blood and spinal fluid were negative. Ophthalmoscopic examination showed abso-

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* From the Anatomical Laboratory of Prof. A. Jakob, Staatskrankenanstalt, Hamburg-Friedricksberg and the Neurosurgical Laboratory of Prof. C. H. Frazier, University Hospital, Philadelphia.

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* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 11, 1930.

1. Professor Bauer, Director of the Hamburg Säuglingsheim, allowed me to use the brain and clinical record in this case.

lutely stiff pupils; the optic nerves were pale and the vessels thin. No choking was found.

Course.—The clinical course was stormy. The stay in the hospital was characterized above all by a "motor restlessness" and by a general rigidity of the musculature. The latter was not constant, but occurred intermittently and was relieved by bromides and ethyl carbamate (urethane). On the day following admission, a strabismus alternans was found, but no nystagmus was demonstrable. The patient was blind and lay with the ocular bulbs rotated downward. After a

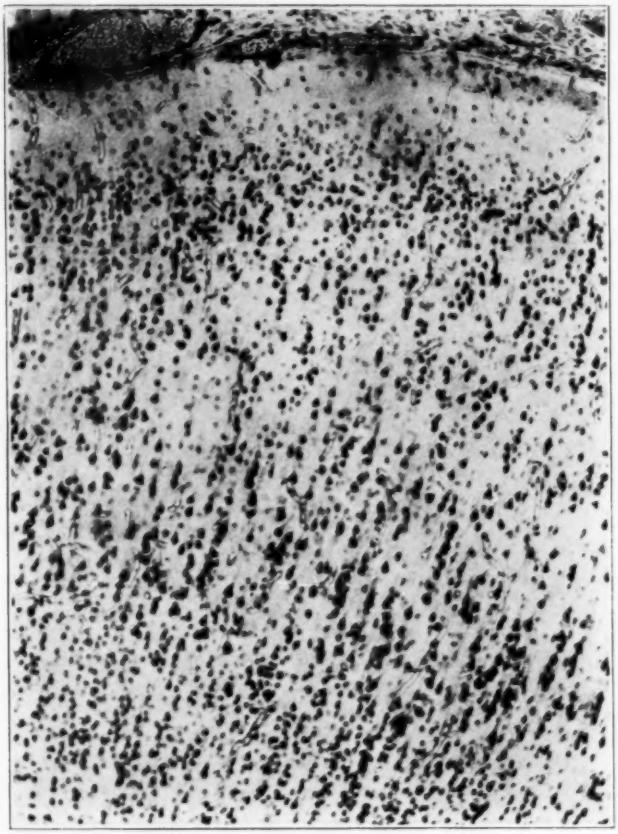

Fig. 1 (case Br.).—Diffuse loss of cells in lamina III of the area frontalis granularis; toluidine blue stain.

cisternal puncture the patient collapsed, with labored breathing, pallor and a weak pulse, but was revived by the administration of caffeine and lobeline, only to relapse once more. She gradually recovered from this attack. The patellar reflexes were much increased during this period, but the abdominal reflexes were absent. The attacks of rigidity occurred daily; their exact nature, however, never became clear. Three days before death, the patient suddenly collapsed; a deep stupor developed; the convulsive attacks ceased, and the child died without recovering consciousness.

Gross Anatomy of the Brain.—The brain grossly showed nothing particularly striking. It was a normal-appearing infant's brain, which was very soft but probably not more so than in a normal case. Beyond this general softness, particularly of the white matter, there was nothing to be observed (Prof. A. Jakob).

Microscopic Examination of the Brain.—The brain was studied by numerous histologic methods. One-half was placed in Mueller's fluid for study of the myelin sheath, and the other half was studied by means of the toluidine blue, fat, van Gieson, Bielschowsky, Perdrau, Holzer, Cajal and Hortega methods. The

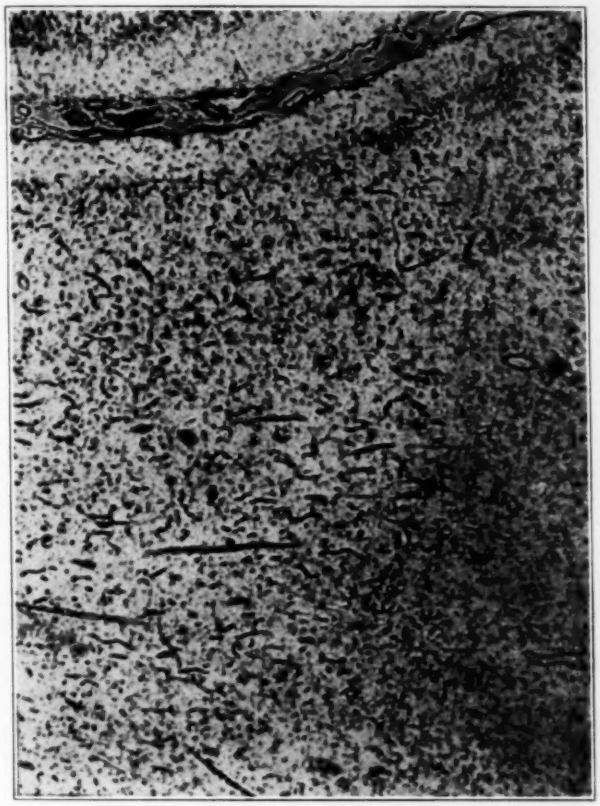

Fig. 2 (case Br.).—Low power view of cortex, showing an area of necrosis; toluidine blue.

brain was cut into blocks, and sections from every part were examined by the methods mentioned. In the frontal region, in the vicinity of the frontal pole of the lateral ventricle, serial sections were made and studied in order to follow the course of the ventricle.

Cortex: Everywhere in the cortex the ganglion cells showed changes. The cells showed round, homogenous nuclei with a well defined nucleolus and with a frayed, ragged, moth-eaten cytoplasm in which no Nissl substance could be made out. In some of the cells the cytoplasm remained only as a small ragged

remnant, irregular in outline and bounded by a cytoplasmic membrane which was often broken. Occasionally, shadow cells were seen. These changes, generalized in the ganglion cells throughout the brain, probably represented cells that had not yet fully matured. The brains of infants aged 7 weeks and 5 and 7 months, showed some cells similar to those described, but these cells were not disseminated throughout the brain.

In various areas of the cortex there was a definite loss of cells in the third lamina. This was a more or less generalized change found in the areae frontalis

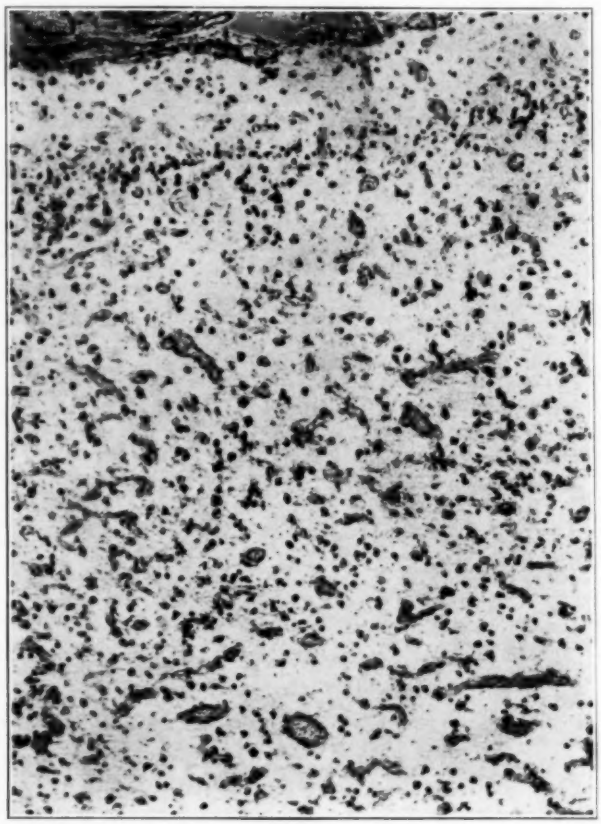

Fig. 3 (case Br.).—Slightly higher power view of the area parietalis, showing incomplete necrosis; toluidine and van Gieson stain.

granularis, frontalis agranularis, temporalis, postcentralis, and parietalis. Within the lamina involved could be found areas in which there was without question a loss of ganglion cells. This can be seen in figure 1, which shows such an area from the area frontalis. In many areas of the cortex, the lower cortical layers were poorly defined, the differentiation between the various layers and the separation of the lamina multiformis from the white matter being very poorly defined. The latter often merged indistinctly into the white cortical substance. On the whole, the cortical architecture was well preserved.

Within the cortex and scattered throughout it, in the frontal, parietal, temporal and occipital regions, were numerous areas which appeared like areas of softening, but which showed a structure different from these. Such cortical areas are seen in figures 2, 3 and 4, under various magnifications. These areas were spread throughout the frontal, parietal, temporal and occipital regions, but were particularly prominent in the areae frontalis granularis, frontalis agranularis, gigantopyramidalis, temporalis, insularis, postcentralis and parietalis. As can be seen from the photographs, they consist of areas within the cortex with markedly

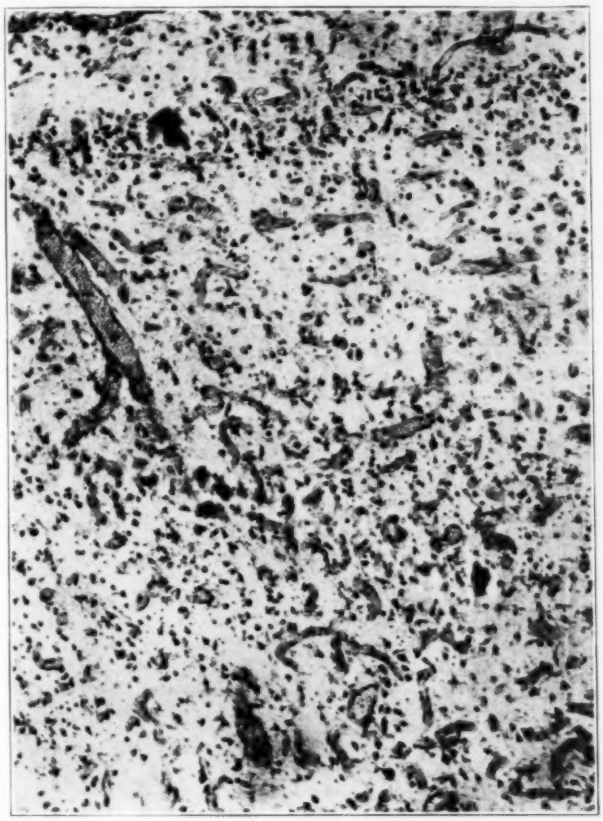

Fig. 4 (case Br.).—The same focus under higher magnification; toluidine blue stain.

dilated capillaries, which are increased in numbers and filled with blood, and have produced so marked a disturbance in the cortical architecture that nothing can be seen of the various layers. Around and among these dilated and increased capillaries the brain substance had a homogeneous, coagulated appearance. Ganglion cells were either markedly decreased in number or almost absent. Scattered throughout the areas, in numbers which varied greatly in the various regions, were ganglion cells with a well defined nucleus, but with a cytoplasm which in most instances was practically gone, and in others remained as a small, round,

ragged band around the nucleus. In a few instances some semblance of the normal contour of the cell could be made out. Usually these areas were small in extent, but sometimes they occupied an entire gyrus. The number of dilated capillaries varied in different regions, being more abundant in some than in others. Astrocytic nuclei, scattered abundantly among the ganglion cells, were numerous in these areas. Gitter cells were occasionally seen.

From the capillaries small buds could be found emanating, and with them a fibroblast or two. In some areas could be found numerous plump astrocytes, rela-

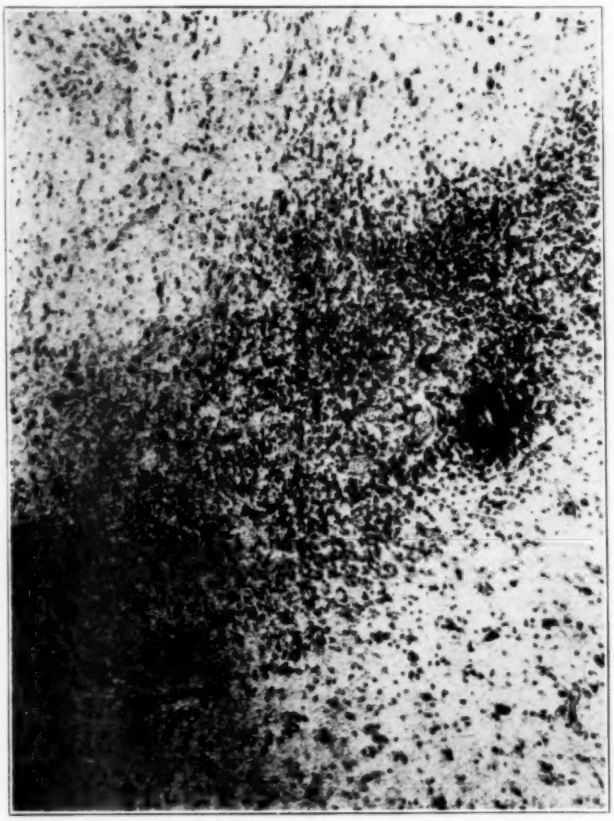

Fig. 5 (case Br.).—Ependymal pocket and area of germinal cells in area parolfactoria; toluidine blue stain.

tively few gitter cells and a few fibroblasts. In other areas there were relatively more astrocytes and microglia cells, and only an occasional gitter cell. The latter might be found in some areas and not in others. These areas of necrosis were confined entirely to the cortex; none was seen in the white substance. The process either stopped sharply at the boundary of the cortex and white matter, or it was separated from the white substance by a relatively intact lamina multiformis. The areas of incomplete necrosis noted throughout the cortex were seen in the course of development in the basal ganglia. They will be described in greater detail.

The area shown in figure 5 is from the parolfactory cortex. This consisted of a large focus of cells infiltrating diffusely into the cortex and disturbing the architecture there. At its periphery was a small pocket lined with several layers of ependymal cells. Most of the cells within the focus consisted of large oval or round nuclei with a well defined nucleolus, little chromatin and no visible cytoplasm. Other cells with spindle-shaped cytoplasm and small dark nuclei were seen. Here and there could be seen elongated nuclei gathered into a sort of roset formation, and occasionally, in the focus, a ganglion cell. The

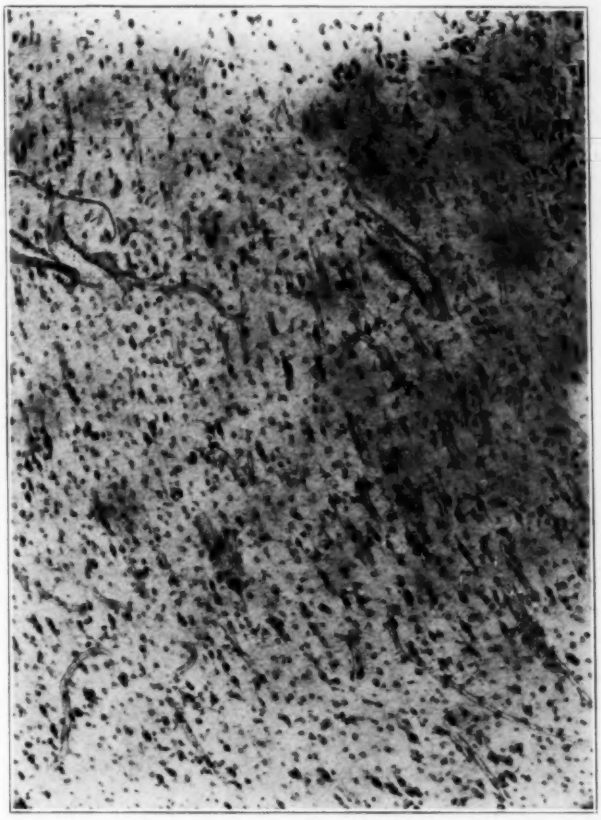

Fig. 6 (case Br.).—Ganglion cells in the white matter; toluidine blue stain.

cells within this focus probably represented germinal cells and spongioblastic elements.

The white matter of the cortex was of great interest. Everywhere, throughout its entire extent, could be seen ganglion cells. These are shown clearly in figures 6 and 7. They were numerous in the subcortical white substance, but were present in equal abundance within the centrum semiovale. As they were traced upward from this area to a gyrus, they seemed to be streaming from the centrum ovale to the cortex, radiating in more or less orderly fashion as they approached the gray substance. Their structure was most varied. Usually the

nucleus was well defined, with a good nucleolus, which was often double. The cytoplasm varied in amount, being more abundant in some cells than in others. It was usually scanty, streaming off the cell in more or less bipolar fashion, or it was seen as an irregular mass without definite shape. As a rule no Nissl substance could be found within these cells, though some contained a semblance of it. Scattered among the ganglion cells were numerous astrocytic nuclei which constituted by far the greater part of the cells within the white matter. In many instances something could be seen of the cell body with the toluidine blue

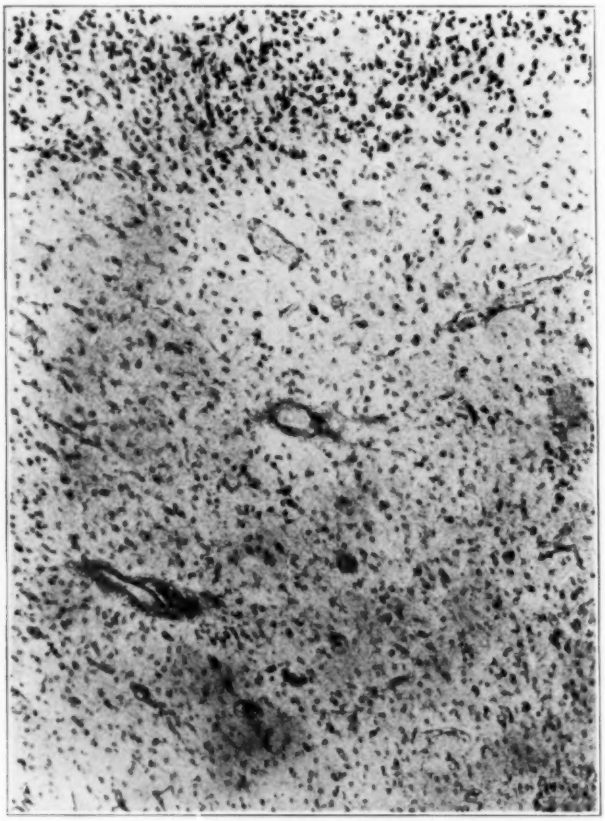

Fig. 7 (case Br.).—Ganglion cells in the white matter; toluidine blue stain.

stain, and almost always the nucleus in these cells was found to be at one pole of the cell while the cytoplasm streamed off the other pole in a sort of rounded eminence from which the processes were emitted. It was an interesting and striking feature of the cortical white matter that the orderly arrangement in rows of the oligodendroglia was entirely missing. The typical oligodendroglia nuclei were lacking, though they were found in great abundance in the internal capsule.

The astrocytes in the white matter, as seen in the gold-sublimate preparations (figs. 8 and 9), were of great interest. They were definitely increased in numbers. Figure 8, which shows a typical area of fibrous astrocytes from the white matter

of the cortex, demonstrates the unquestionable glial hyperplasia. The cells themselves were striking. The nuclei were for the most part eccentric, situated at one pole of the cell, and often placed tangentially so that they did not seem part of the cell. The protoplasm of these cells had a spongy weblike appearance, more typical of the protoplasmic than of the fibrous astrocyte. Sometimes this spongy appearance filled the entire cell, sometimes only a part of it, and occasionally it was not present at all. Intracellular fibrils were not abundant in these cells, and when seen were usually present in the sucker process which gave rise to the sucker foot. Most interesting of all were the processes which emanated from these cells. Instead of the long, sweeping, linear, dichotomizing processes which characterize the normal fibrous astrocyte, these cells, as can be seen clearly in figure 9, had short, slender, fine processes which began to branch richly as soon

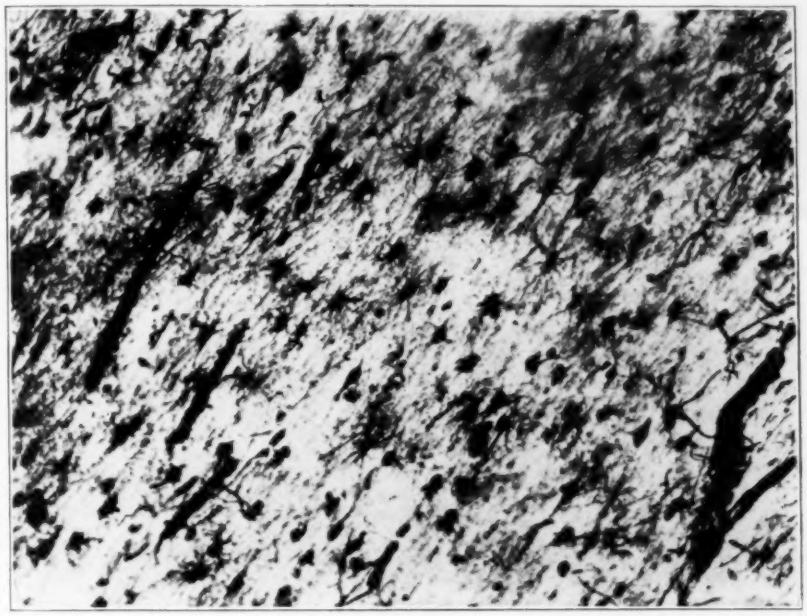

Fig. 8 (case Br.).—Immature astrocytes in the white substance; Cajal's gold chloride-sublimate method.

as they left the cell. The end branches were fine and slender. In most instances the cell protoplasm and body came off one pole of the cell. Often the sucker process in these cells was thick and stout, far out of proportion to the size of the cell. These astrocytes were unquestionably immature cells and corresponded exactly to the juvenile type of neuroglia described by Cajal. In contrast to the neuroglia cells in the cortex, those of the spinal cord appeared much more like adult fibrous astrocytes.

Of particular interest in this case were the subependymal periventricular foci, which are seen in figures 10, 11 and 12. They were always situated in the white matter and in the subependymal region. Some lay close under the ependyma (fig. 10) and others (fig. 11) lay fairly deep in the periventricular white substance. All of these foci lay in the frontal region of the brain; none was found

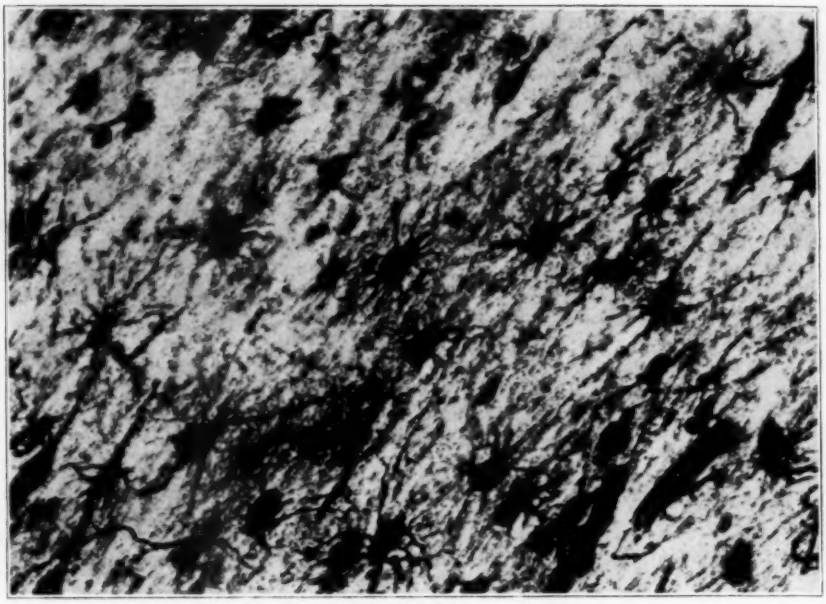

Fig. 9 (case Br.).—Same as figure 8 under higher power.

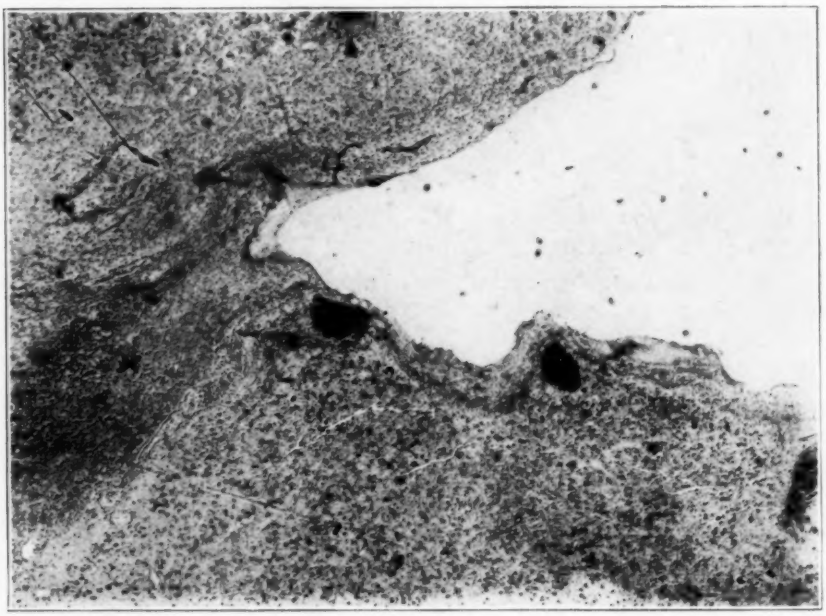

Fig. 10 (case Br.).—Subependymal areas of germinal foci and area of giant cells; toluidine blue stain.

in the posterior portions of the ventricle. The foci were arranged in small or large, round heaps (figs. 10 and 12), in elongated piles (fig. 11) or in long finger-like processes (fig. 11). In areas of great abundance they were gathered into a large irregular heap. Very often they were seen gathered into small groups in a perivascular arrangement (figs. 11 and 12). In every case the vessel was a vein. Usually the cells were grouped just outside the vessel, but sometimes a group could be seen within a perivascular space. In one instance, a small focus was found grouped around an ependymal pocket. While the vessels shown in the

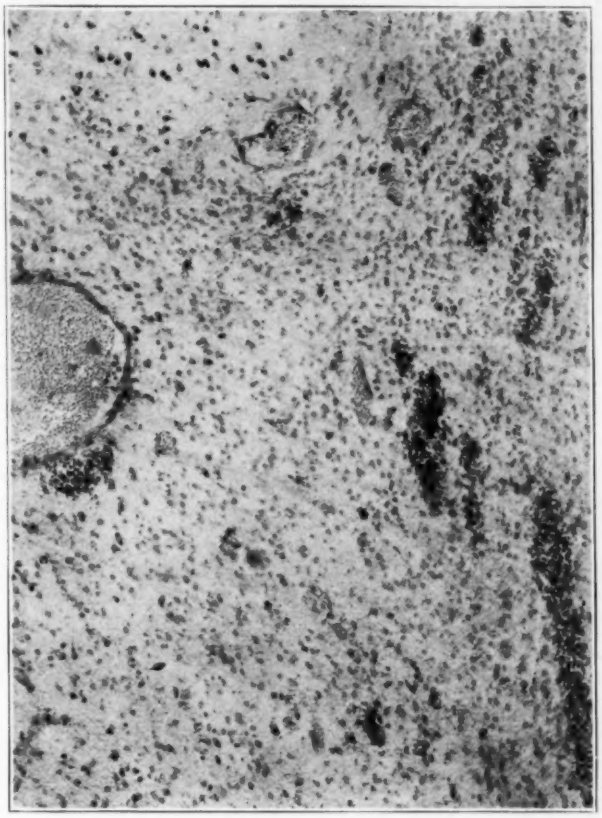

Fig. 11 (case Br.).—Periventricular and perivascular collections of germinal foci; toluidine blue stain.

illustrations are fairly large, this was not always the case; often small groups of these cells could be found gathered around a small capillary. The cells within these foci consisted of bare nuclei around which no cytoplasm was visible. The nuclei contained a well defined nucleolus but were poor in chromatin. In most of them there were only a few fine chromatin granules; in others a large chromatin content was visible. For the most part, the nuclei were round, but elongated, oval or roughly rectangular shapes were also found. These foci were so-called "germinal centers" the significance of which will be discussed later.

In figure 10, at *X*, can be seen a group of cells which, when seen under a higher power (fig. 13), can be identified as giant cells. They lay at the pole of the anterior horn of the lateral ventricle within the frontal lobe. As can be seen in the very low power photograph (fig. 10), these cells were concentrated in a large focus at the ventricular pole. The cells contained from three to six or eight nuclei, arranged circularly around the cell or in long rows. Among them were cells containing a single nucleus. The protoplasm was abundant, the cells having a round, oval or even spindle-shaped appearance. These cells could be followed

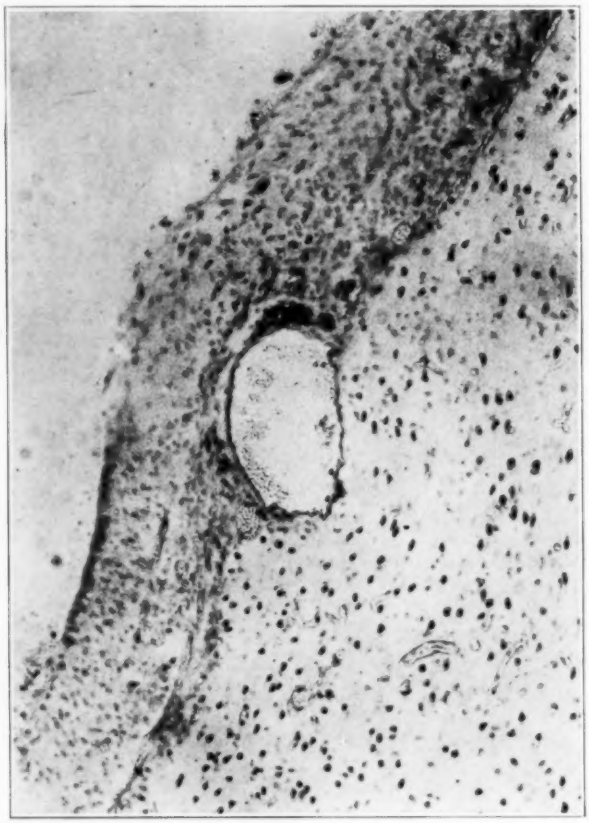

Fig. 12 (case Br.).—Perivascular collections of germinal foci; toluidine blue stain.

under the ventricular ependyma, where they became fewer and fewer as they lay under the ventricle lining, usually in a single row of scattered cells. In the white matter they merged more or less definitely with the surrounding brain substance, and yet they remained distinct from it. Around them they had evoked a marked glial response, the white matter consisting chiefly of neuroglia nuclei with many fewer ganglion cells than in other portions of the white substance.

Fat was present in the white matter in great abundance. It was found concentrated in foci within cells (fig. 14), or it was spread diffusely throughout the

white substance. It was often found also in the adventitial sheaths of the vessels (fig. 15).

Axis cylinders were definitely fewer in the white substance. In some areas they were almost entirely absent; in others they were markedly decreased in number, while still other areas showed only a moderate loss. They were of extraordinary fineness. In areas where the axis cylinders were abundant, foci in which they would be entirely absent might be found. In addition, there were larger areas, where there were no axis cylinders. Secondary changes, such as swelling, fragmentation and granulation, were frequent.

In figures 16 and 17 is seen an interesting observation in a pial artery over the frontal cortex. This vessel showed a focal hyperplasia of the intima which took a metachromatic tint in the toluidine blue preparation, but in which there

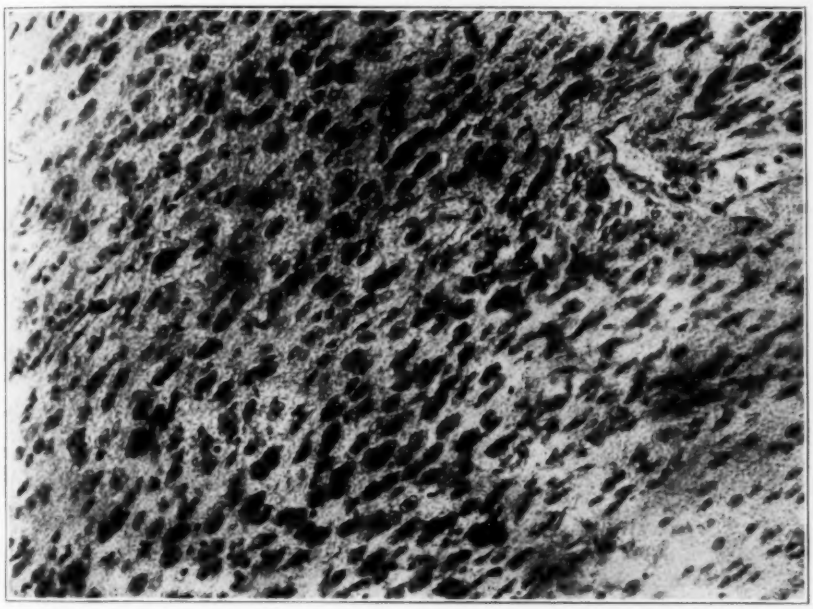

Fig. 13 (case Br.).—Giant cells at the terminus of a ventricle; toluidine blue stain.

was no deposit of fat. The membrana elastica was intact (fig. 18). This can be interpreted as an early arteriosclerotic change.

Basal Ganglia and Brain Stem: In these regions there were definite changes. In the caudate, putamen, pallidum and pons were areas similar to those found in the cortex. In figures 18 and 19 are shown two areas within the caudate and pallidum. The necrotic areas in the pallidum were scattered throughout this nucleus, so that only scattered islands of relatively normal tissue remained. These presented different appearances in different parts of the pallidum, depending on the extent of the damage and on the age of the lesion. In some, rich sproutings in the form of small buds could be seen coming from the capillaries, forming new vessels. The endothelium of the capillaries was usually normal, but in some cases it was definitely swollen. Close to the walls of the capillaries could be seen fibroblasts.

These were numerous around some vessels and either few or absent around others. Occasionally fibroblasts could be seen free in the tissue. Astrocytes were numerous in these areas. Microglia were also numerous, but less so than the astrocytes, and in some instances a definite rod cell could be identified. Occasionally, gitter cells could be seen. Often the astrocytes in these areas had a definite metachromatic tint, and within their cytoplasm were coarse metachromatic granules. In other areas of necrosis within the pallidum the cell picture was somewhat different. Here, the vessel proliferation was not so active, but the cell

Fig. 14 (case Br.).—Fat in the pallidum; Fett Ponceau stain.

proliferation was more pronounced (fig. 20). In some places the cells consisted chiefly of astrocytes, and in others of microglia. Even here, gitter cells were rarely encountered. An active perivascular proliferation of astrocytes was seen in this region. Even in the Nissl picture the protoplasm of the cell was plump, full and metachromatic. From these perivascular areas, the astrocytes could be followed out into the surrounding tissue in great numbers. The latter foci with fewer capillaries and greater cell reaction, chiefly of astrocytes, represented later stages in the same process described in the cortex and in other parts of the pallidum.

The caudate and putamen contained foci similar in all respects to those in the pallidum.

In the pons (fig. 21) were similar areas. These showed typical capillary proliferation with buddings and with an occasional swollen endothelial cell. Ganglion cells were markedly degenerated and atrophic and often consisted of mere shadows. Astrocytes were common. Microglia cells were seen in great numbers, but gitter cells were infrequently encountered. Around the foci could be seen a definite hyperplasia of astrocytes.

Fig. 15 (case Br.).—Vessels infiltrated with fat; Fett Ponceau stain.

In the thalamus (fig. 22) was seen a true area of softening, the only one found in a careful search of the entire brain. This area was extensive and involved the median nucleus and part of the lateral thalamic nucleus. It showed fresh softening with numerous capillaries, dilated and extending throughout the area, while among them were great numbers of gitter cells. Very few fibroblastic elements were seen, and no wall had been formed around the focus. The demarcation from the healthy substance was indistinct. In addition to this focus there were other foci similar to those described in the cortex, striatum and pallidum. One of these was very large, while other small ones were scattered throughout

the thalamus. In these foci there was a loss of ganglion cells. Atrophic, shrunken cells could be seen but they were infrequent. The cellular elements among the capillaries consisted almost entirely of astrocytes which seemed to be relatively increased in these foci. The thalamic substance in the areas in which the cells were laid had a homogeneous, gelatinous appearance. Scattered throughout the thalamus also were dilated capillaries which seemed to be accompanied by an increase in astrocytes, but around which the number and character of the ganglion cells remained normal.

Fig. 16 (case Br.).—Arteriosclerotic plaque in pial vessel; toluidine blue stain.

Throughout the basal ganglion region, fat was seen in great amounts (figs. 23 and 24). It was more abundant in the striatum, but was present also in the pallidum and thalamus. It was found in foci within cells as seen in figure 24, which showed a large focus, but it was also found as a diffuse infiltration within the tissue. It was found, in addition, in the walls of the vessels in this region, both in the larger vessels and in the capillaries.

The cerebellum showed no foci within its cortex, but the white matter was mildly populated with ganglion cells, just as in the cerebrum, and the fibrous

astrocytes were much increased. The Purkinje cells were normal, and the cerebellar nuclei were without change.

Myelin Sheaths: There was a marked loss of myelin in the entire cortex and in the striopallidum (fig. 25). A large part of the thalamus was completely demyelinated. The corpus callosum was poor in myelin sheaths, and the white matter was somewhat poorer in myelin than is usual in a normal child. The process consisted, therefore, of a highgrade demyelinization or lack of proper myelinization of the cortex, striopallidum and thalamus and to some degree of

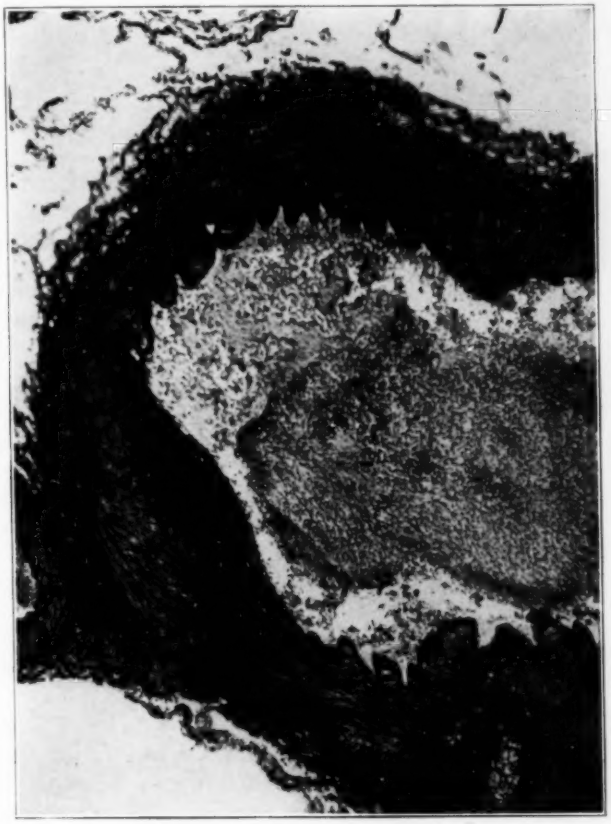

Fig. 17 (case Br.).—The same vessel in van Gieson elastic stain.

the corpus callosum and white matter. Other portions of the brain appeared normal.

Summary.—The patient, an infant, aged 4 months, apparently developed normally, but in the third month of life generalized convulsions, hyperkinesis and attacks of general rigidity of the entire musculature developed. The only physical abnormalities found were hyperactive patellar reflexes.

Grossly, the brain showed nothing save a generalized softness which is normal for an infant's brain.

Microscopically, the changes in the brain can be divided into two categories: (1) structural changes and (2) developmental changes. The first type was represented by peculiar necrotic areas spread diffusely throughout the frontal, parietal and occipital regions and through the caudate, putamen, pallidum, thalamus and pons. These were more pro-

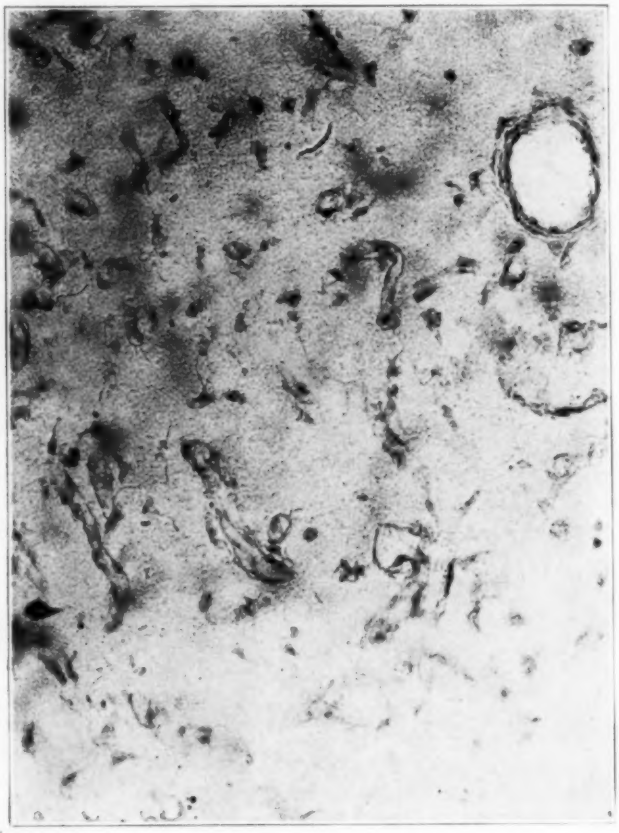

Fig. 18 (case Br.).—An area of incomplete necrosis in the caudate nucleus; toluidine blue stain.

nounced in some places than in others, the whole producing a diffuse damage which tended to be more marked in some areas. The areas consisted of dilated capillaries, definitely increased in numbers, from which numerous capillary buds were springing, accompanied by a marked loss of ganglion cells; scattered among the capillaries in varying relations were astrocytes, microglia and fibroblasts. The latter were never very frequent. In the younger areas the astrocytes were less

numerous and the microglia relatively more numerous. In the older foci the astrocytes were markedly increased in number. Gitter cells were infrequent, and often they were absent.

The striking feature in the cellular reaction within these areas was the predominant participation of the neuroglia, with the microglia assuming a relatively less important rôle even in the younger areas. The mesodermal elements were active in the multiplication of capil-

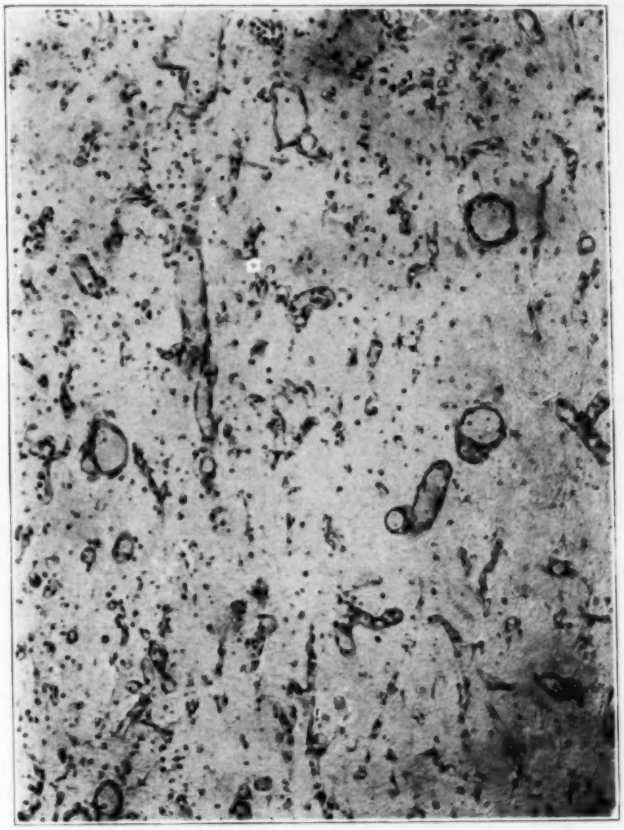

Fig. 19 (case Br.).—A similar focus in the pallidum; toluidine blue stain.

laries, but fibroblastic proliferation was mild, and there was no diffuse deposit of connective tissue within the areas. One can therefore state with safety that the process was chiefly neuroglial, with a minor participation of the mesodermal structures. In many regions there was a diffuse cell loss in the third lamina. The process was confined to the gray matter of the cortex and subcortical areas, and in no instance did it spread over into the white substance. From this it was always sharply

demarcated in areas involving the entire width of the cortex, or it was separated from the white substance, in some cases by a relatively intact lamina multiformis. There was demyelinization of the cortex, striopallidum and thalamus.

The entire brain showed evidences of developmental retardation for a child of 3 months. The entire subependymal region showed a layer of spongioblastic cells several layers thick and well demarcated from the

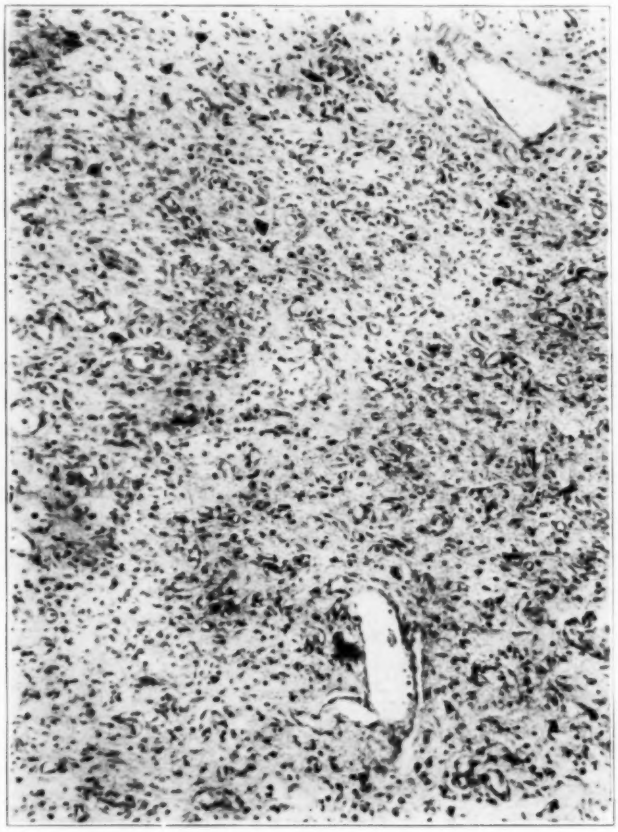

Fig. 20 (case Or.).—Gliosis in the pallidum; toluidine blue stain.

underlying white matter. Scattered throughout the entire course of the frontal portion of the ventricle were foci of cells situated in the subependymal white matter or arranged around vessels. At the frontal pole of the ventricle was a large focus of giant cells. The entire white matter throughout the brain showed the presence of large numbers of immature ganglion cells, numerous astrocytes and a failure of oligodendroglia cells. By proper stains it could be determined that the astrocytes were definitely hyperplastic, and that they were not typical adult fibrous astrocytes but immature juvenile forms with definite characteristics. In

the white matter there was fat in abundance, spread diffusely or concentrated in foci. The axis cylinders were decreased in number in the white substance; in many areas they were almost absent. In the parolfactory area was a large focus of germinal cells in the midst of which was an ependymal-lined pocket, and over the frontal cortex was a pial vessel with localized intimal proliferation. Many regions of the cortex showed a loss of cells in the lamina pyramidalis.

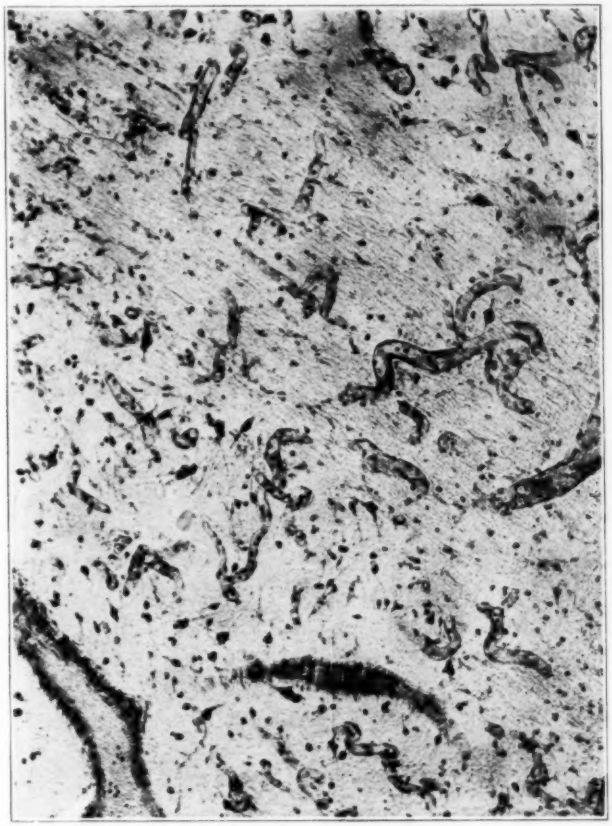

Fig. 21 (case Br.).—An area of incomplete necrosis in the pons; toluidine blue stain.

COMMENT

From the pathologic standpoint there are two aspects to this case, one concerned with the areas already described in the cortex, basal ganglia and pons, and the other with the various evidences of developmental disturbances found throughout the brain.

Diffuse Areas of Necrosis.—These are seen in figures 2, 3, 4, 18, 19 and 21. They deserve further amplification. Their outstanding

feature consists in their strict confinement to the gray matter of the cortex and basal ganglia. Nowhere do they spread into the white substance. In the instances in which the entire width of the cortex is involved, the process is sharply demarcated from the underlying white matter, and in the instances of incomplete involvement of the cortex, a more or less intact lamina multiformis separates the process from the white substance. Similarly with regard to the basal ganglia, never does

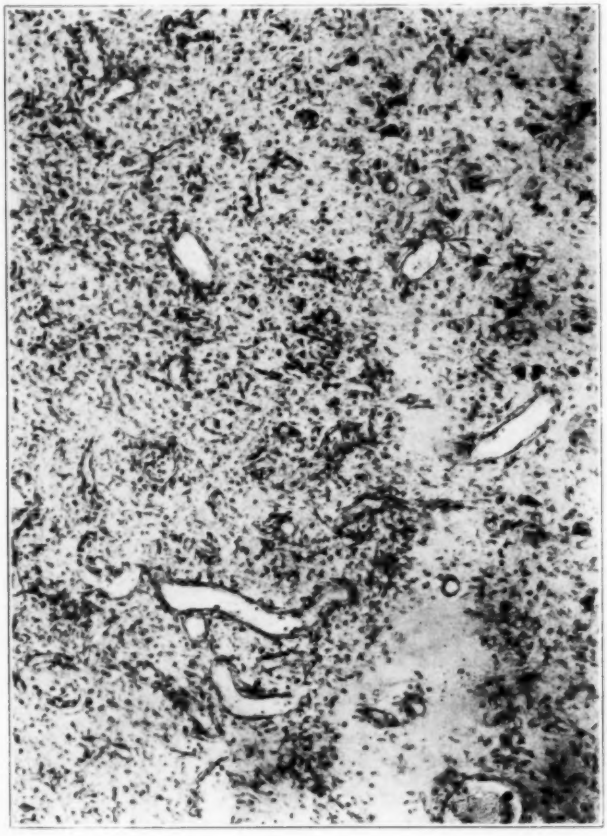

Fig. 22 (case Or.).—An area of softening in the thalamus; toluidine blue stain.

the process involve the adjacent white matter. The pathologic process is scattered diffusely throughout the frontal, temporal, parietal and occipital cortex, but within certain areas in these regions it is accentuated and more extensive. So also is it more pronounced in the basal ganglia. The pathology implicates diffusely the putamen, caudate, pallidum and thalamus, but within certain areas is more pronounced. It is more pronounced in the basal ganglia than in the cortex. One

can speak, therefore, of a process which is diffuse in the gray substance of the brain, but which is more marked within certain areas of the cortex and in limited areas of the basal ganglia region.

The microscopic characteristics of the process are striking. The underlying feature is a necrosis of brain tissue with a marked loss of ganglion cells. The reaction to this process consists of capillary proliferation, marked neuroglial hyperplasia, mild microglial response, very

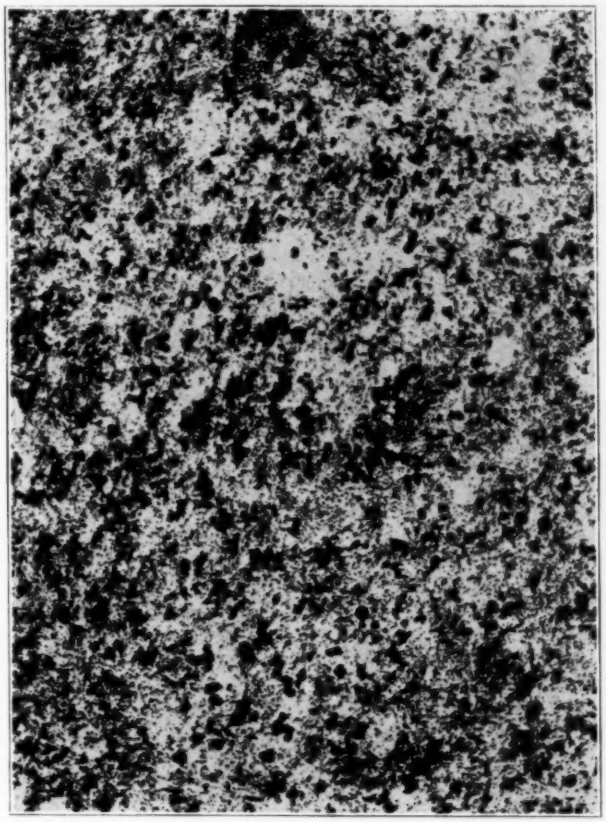

Fig. 23 (case Br.).—Fat in the striatum; Fett Ponceau stain.

mild fibroblastic participation and only rare gitter cells which are not present in every area. The reaction to the process is therefore chiefly a neuroglial response, with a moderately active participation of some mesodermal elements, the capillary endothelium, and a very mild response of other mesodermal elements, the microglia and fibroblasts. No diffuse connective tissue response is anywhere evident, so that a connective tissue network is totally lacking in the areas involved.

This type of disorder has been described by Jakob [2] as an incomplete necrosis, the histologic process consisting, in the early stages, of a loss of ganglion cells, and increase in capillaries, a hyperplasia of microglia and astrocytes and an occasional gitter cell. In the later stages the process is more marked, with an increase in the neuroglial elements which dominate the picture. The reaction is chiefly neuroglial, but as

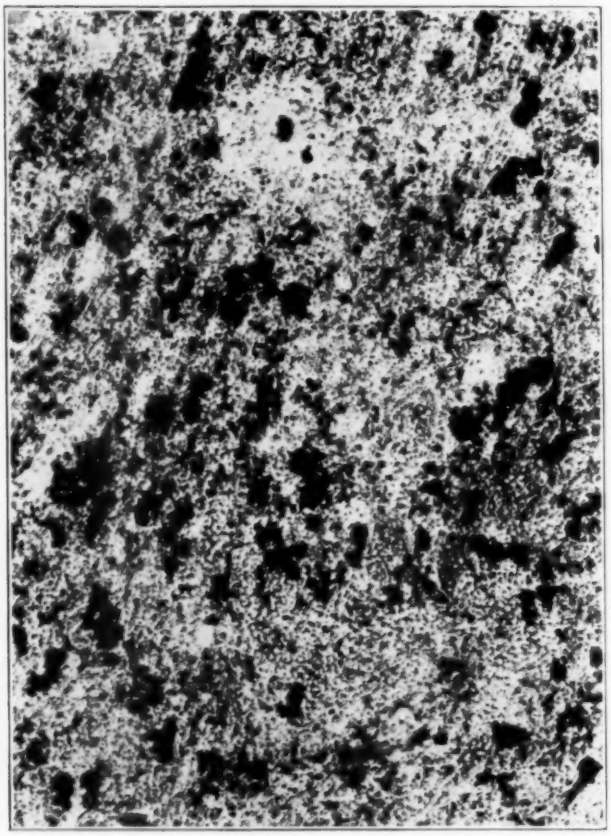

Fig. 24 (case Br.).—Figure 23 under higher power.

Jakob pointed out the reaction depends on the size of the area, the acuteness of the injury and the nature of the fundamental illness. With these factors playing a varying rôle, the number of forms which these incomplete necroses may assume is manifold. The mild participation of the mesodermal elements in the process in my case differentiates it

2. Jakob, A.: Anatomie und Histologie des Grosshirns. Vienna, Franz Deuticke, 1927, vol. 1.

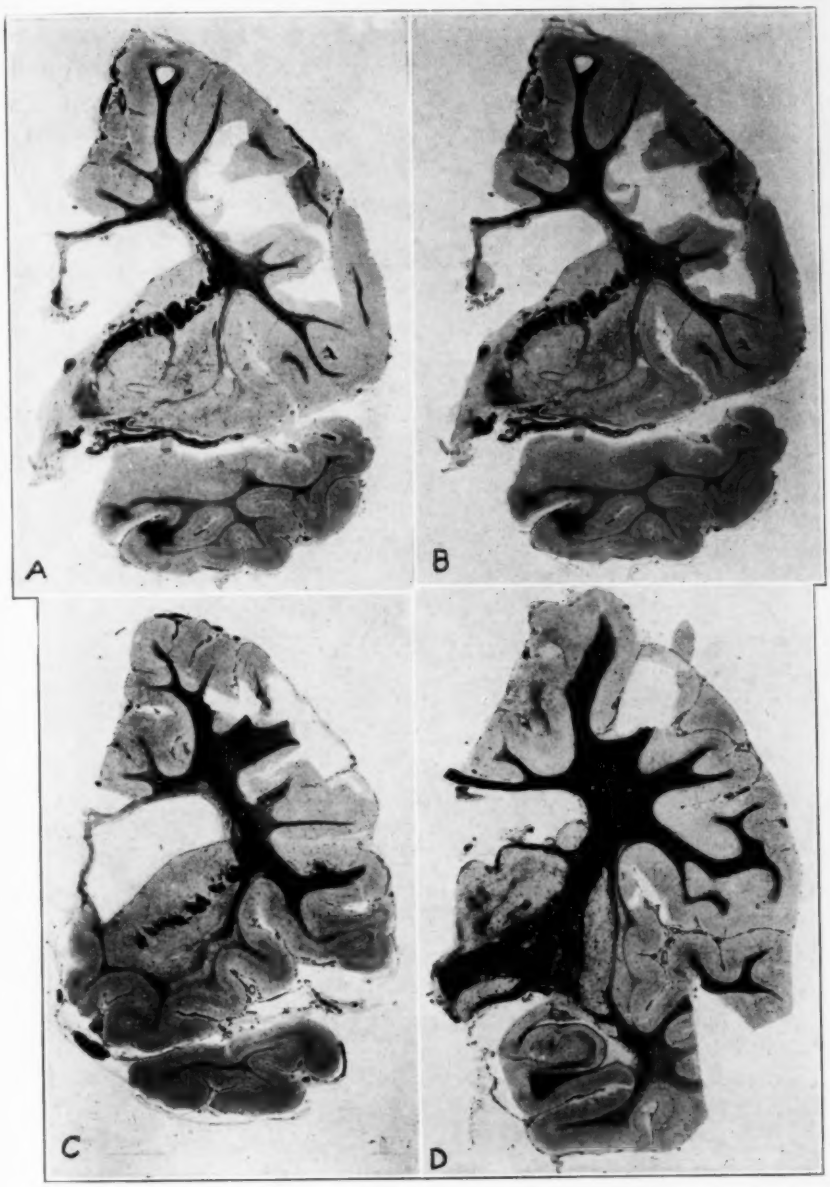

Fig. 25 (case Br.).—Demyelinization of the cortex and striopallidum; myelin sheath stain.

from those described by Nissl,[3] Hoche,[4] Farrar,[5] Spielmeyer[6] and Saito.[7] In the necroses which these authors described, the participation of the mesodermal elements is so active that a diffuse connective tissue network is laid down. Gitter cells are extremely numerous, and actual softening occurs later. In my case the fibroblastic elements are always in the background. They never play an important part in the process. Only in one area, in the thalamus where there is a frank area of softening, is there an outspoken mesodermal-glial reaction similar to that described by the authors cited.

The etiology of the process is not clear in my case. It cannot be stated definitely. Such incomplete necroses occur as the result of vascular processes of all sorts, by pressure from tumors and in toxic conditions. In Jakob's case, an encapsulated tumor of the temporal lobe produced incomplete necroses in the cortex and white matter of the calcarine area at some distance from the pressure of the tumor. Whether the process is due to vascular or toxic injury it is impossible to say. Certain features suggest that the process may be toxic. Its confinement to the gray substance of the brain, with a dilatation of capillaries and loss of ganglion cells is similar to the state of affairs in carbon monoxide poisoning, though the histologic picture is by no means the same. The selection of the gray matter in both instances is striking, although the localization of the process is different in the two instances. It is well known that carbon monoxide poisoning produces a marked softening in the pallidum, but recent studies have shown that the cortex may also be implicated in many instances, either with or without a simultaneous disease of the pallidum. Grinker,[8] indeed, reported a case in which the white substance was very severely involved. At any rate, the exquisite selection of the gray substance in carbon monoxide poisoning, which is frankly a toxic affair, compared with a similar selection in my case suggests the possibility of a toxic factor in the production of the process.

3. Nissl, F.: Zur Histopathologie der paralytischen Hirnerkrankung, in Histologische und histopathologische Arbeiten über die Grosshirnrinde, 1904, vol. 1, p. 1.

4. Hoche, F.: Experimentelle Beiträge zur Pathologie des Rückenmarkes, Arch. f. Psychiat. **30**:32, 1897.

5. Farrar: On the Phenomena of Repair in the Cerebral Cortex, in Nissl, in Histologische und histopathologische Arbeiten über die Grosshirnrinde, 1908, vol. 2,

6. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

7. Saito, S.: Experimentelle Untersuchungen über Nekrose, Erweichung, und Organisation an der Hirnrinde des Kaninchens, Ztschr. f. d. ges. Neurol. u. Psychiat. **96**:539, 1925.

8. Grinker, R.: Bilateral Softening of the Lenticular Nucleus in Carbon Monoxid Poisoning, Ztschr. f. d. ges. Neurol. u. Psychiat. **98**:433 (Sept.) 1925.

This seems the more possible in view of the slight similarity in the histologic pictures in the two instances. Further than this, however, it is impossible to go.

The process in my case, confined as it is to the gray substance of the cortex and basal ganglia, is in frank contrast to that in diffuse sclerosis. In the latter, the process is confined almost entirely to the white matter of the brain, except in exceptional areas in which it may creep over into the gray substance to some extent. The gray matter remains on the whole intact; the pathologic process is confined entirely to the white matter. On the other hand, the pathologic process in my case is entirely in the gray matter. What pathologic change is present in the white matter is apart from that in the gray substance.

A similar process has been described by Freedom,[9] from the laboratory of Jakob. The patient in his instance was an idiot, aged 19, with athetotic movements, epileptiform attacks, hypertonia and hyperextensibility of the extremities, and hyperkeratosis of the skin of the entire trunk. He died of bronchopneumonia. The brain showed a progressive, degenerative process spread diffusely over the entire cerebral cortex, but with all its diffuseness, showing a tendency to be focalized in certain areas. Its chief area of localization was behind the fissure of Rolando in the posterior central gyrus, the posterior insula, the occipital and temporal lobes, and in the hypothalamus, thalamus, pallidum and striatum. Histologically, the process was characterized as a severe, progressive, parenchymatous disease in which the fibers of the entire cortex were practically lost, while putamen, caudate, pallidum and hypothalamus showed a severe loss of fibers, but no status marmoratus. The cortex showed an enormous proliferation of microglia of both a progressive and a regressive nature, with fat deposits within them. Accompanying this was a proliferation of protoplasmic neuroglia. Everywhere was a laminar degeneration in the third lamina, but despite this there was in many areas a status spongiosus of the entire width of the cortex. In the areas most severely injured, the vessels were infiltrated with round cells in the sense of an abortive inflammation. The basal ganglia showed changes similar to those in the cortex. The case showed, therefore, a peculiar, severe, diffuse, progressive degeneration of almost the entire cortex, extensive areas of the thalamus and hypothalamus, and in part the striatum and pallidum. Freedom considered the possibility of an endocrine disturbance as likely considering the lack of development of the endocrine glands and the hyperkeratosis of the skin.

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9. Freedom: Ueber einen eigenartigen Krankheitsfall des jugendlichen Alters unter dem Symptomenbilde einer Littleschen Starre mit Athetose und Idiotie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **46**:196, 1927.

The case of Freedom is similar to mine in the exclusive involvement of the gray substance of the brain with a tendency to focalization in some areas, in the generalized rarefaction of the third lamina and in the marked neuroglial reaction accompanying the process. Histologically, the two cases differ in the lack of capillary proliferation in Freedom's case, and the minor rôle played by the microglia in my case. Freedom's patient lived to be 19 years of age and died of an intercurrent infection. The patient in my case died at the age of 5 months. The difference in the histologic picture may therefore be due to the chronicity of the process. Clinically the two cases are similar.

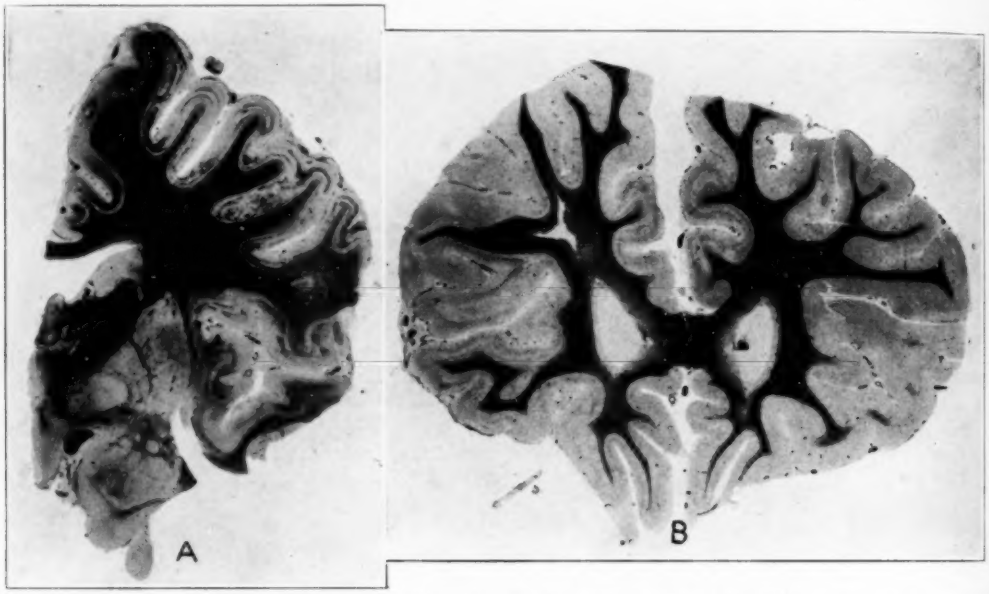

Fig. 26 (case He.).—Demyelinization in the cortex and striopallidum; myelin sheath stain.

The point of extreme importance in both instances lies, however, in the localization of a process exclusively within the gray substance of the brain.

Somoza [10] described another case which simulates mine closely. His patient was a child, aged 8 months, who was markedly asphyxiated at birth, in whom, just as in my case, severe hyperkinesia, marked opisthotonos and choreiform movements developed. The child had to be resuscitated at birth by several hours of artificial respiration. Microscopically, the brain showed a process similar to that described in the case of Freedom and in mine: a marked loss of fibers in the entire

10. In a publication to be reported from the laboratory of Prof. A. Jakob.

cortex (fig. 26) with a similar loss in the caudate, putamen, pallidum and hypothalamus. There was loss of cells in the pallidum (fig. 27) and hypothalamus (fig. 28), just as in my case. In Somoza's case, an additional feature was present, namely, a fatty degeneration of the substantia nigra (fig. 29). The entire cortex, but particularly the area frontalis granularis and agranularis, showed a diffuse loss of cells in the third lamina. The cornu ammonis was also affected. The process

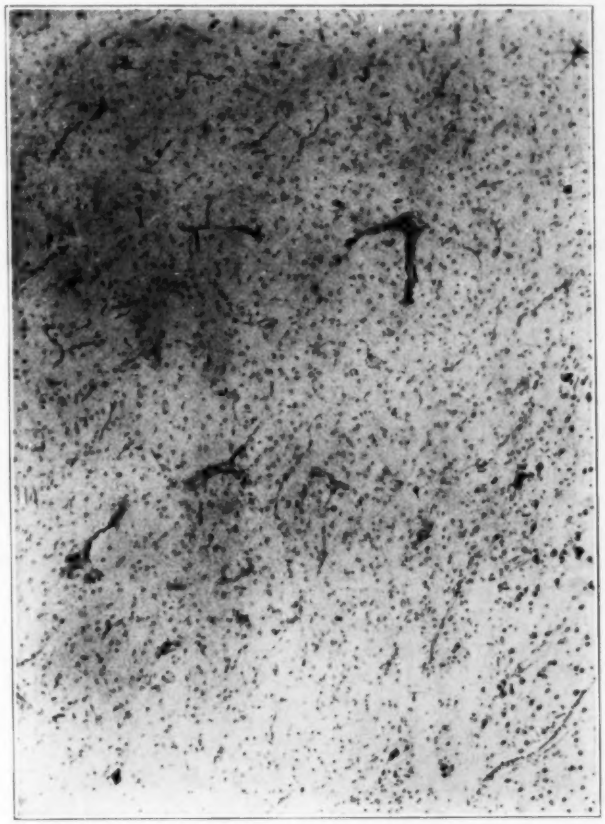

Fig. 27 (case He.).—Loss of cells in the pallidum; toluidine blue stain.

was therefore, as in Freedom's case and mine, a diffuse degenerative process of the cortex and subcortical gray matter with loss of fibers and diffuse loss of cells.

The etiology in Freedom's case is not clear. In the case of Somoza, asphyxia was a definite factor in the production of the pathologic process.

Developmental Defects.—Of equal interest are the developmental disturbances which are found in abundance in the brain described.

These consist of the numerous subependymal and periventricular foci, the large focus in the parolfactory cortex, the ganglion cells scattered throughout the white matter of the cerebrum and cerebellum and the numerous giant cells found in large foci at the pole of the anterior horn of the lateral ventricle. These observations are striking in themselves, but they gain in interest when one considers the light which they throw on certain developmental aspects of the infant brain.

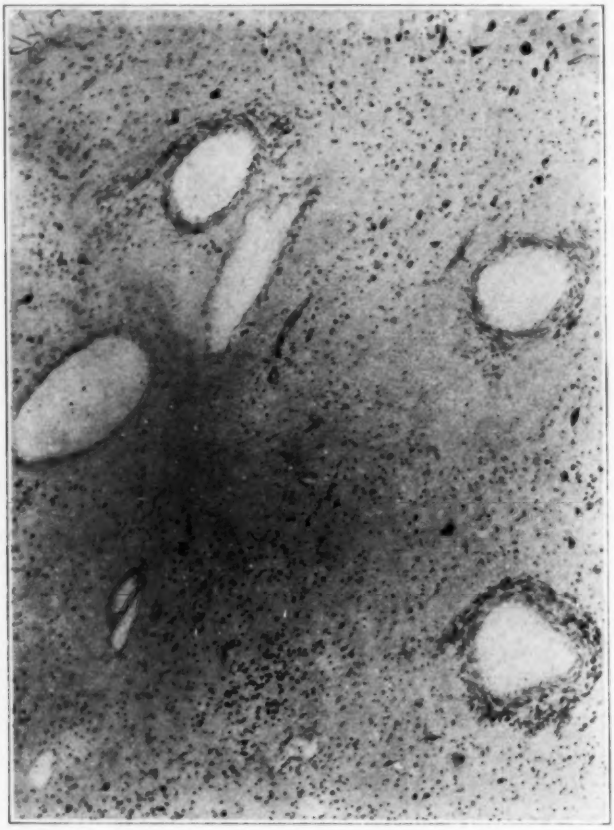

Fig. 28 (case He.).—Loss of cells in the hypothalamus; toluidine blue stain.

Knowledge of the development of the brain in the later months of embryonic life and during the first months of postembryonic development is still insecure in many important details. In order to facilitate the study and interpretation of my specimens, constant careful comparisons were made with the brains of normal infants. Three such brains from infants, aged 7 weeks, and 5 and 7 months, were studied in the laboratory of Professor Jakob, and in the evaluation of the

observations in my case a careful comparison with the normal was made, area for area.

The Subependymal Foci.—Chief among the developmental defects were the cellular foci illustrated in figures 10, 11 and 12. These consisted of round, elongated or large diffuse collections of small, dark-staining nuclei which were situated just under the ependyma or in the periventricular white matter and often were found in small collections

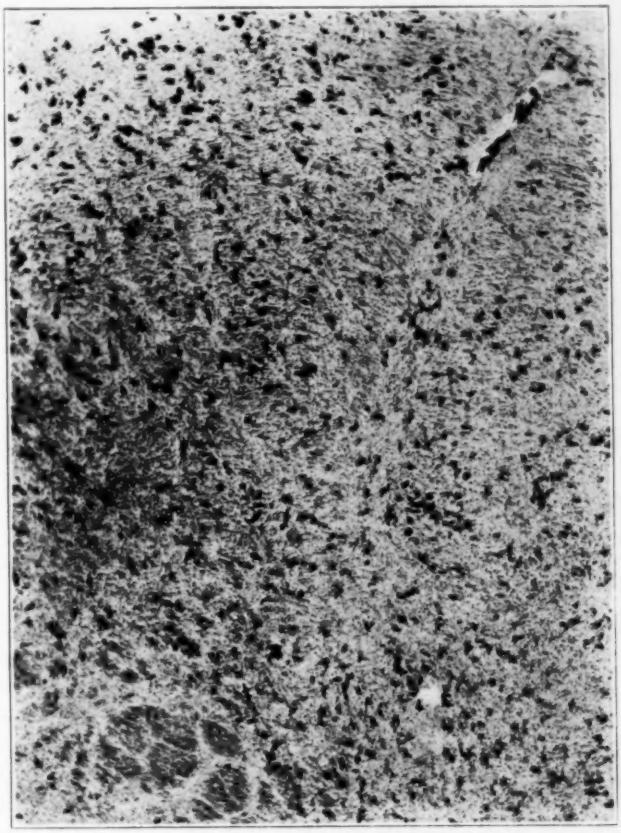

Fig. 29 (case He.).—Fat in the substantia nigra; Fett Ponceau stain.

around vessels. These foci were first described by His. They were described later in greater detail by Ranke [11] who was able to trace their development. In the first four months of fetal life the ventricular

11. Ranke, O.: Beiträge zur Kenntnis der normalen und pathologischen Hirnrindenbildung, Beitr. z. path. Anat. u. z. allg. Path. **47**:51, 1910; Ueber eine besondere Form von Entwicklungsstörung der menschlichen Grosshirnrinde, Neurol. Centralbl. **24**:683, 1905; Ueber Gewebsveränderungen ein Gehirn luetischer Neugeborener, ibid. **26**:112, 1907.

germinal layer consists of a uniform, homogeneous layer of cells. At the end of the fourth and in the beginning of the fifth month a change occurs, consisting of a condensation of the cellular elements in the region of the ventricle and the formation of germinal centers (Keimbezirke). At the end of the fourth month, Ranke found germinal cells around all the large vessels penetrating into the matrix from the ventricle. These surrounded the vessel in a mantle layer, often from six to eight cells in thickness, and could be followed along the vessel during its entire course through the matrix. During the fifth and sixth months these formations are found with great frequency. In this stage of development, however, foci of germinal cells are found in round or elongated islands within the matrix, having no relation whatever to the vessels. Ranke called these foci vascular and ventricular germinal centers. He did not find these foci at the end of the seventh embryonic month, nor was he ever able to find them in the brains of new-born infants. Their function, therefore, is operative only during a very short period in the course of development. Wohlwill [12] agreed essentially with Ranke in stating that these vascular and ventricular germinal centers are never absent in brains from the sixth to the eighth fetal months. He expressed the belief that they are less constant after the normal birth period, and he found them with great frequency in still-born children. He studied a series of seventy-seven brains of infants in which he was able to follow the fate of the cells for varying periods after birth. Ceelen [13] confirmed his observations and stated that he found these foci in the brains of 50 per cent of normal infants born at term. Schwartz [14] demonstrated that they are richest in the frontal lobes. There is therefore little question that these germinal centers, though disappearing chiefly at the end of the seventh or at the beginning of the eighth fetal month, often persist and are found in infant brains at birth. However, as Wohlwill pointed out, a persistence of these foci in the first months of extra-uterine life, frequently seen, is definitely pathologic. Ranke also believed that if the foci are seen at birth they are pathologic, since they should all have disappeared by the end of the seventh month.

The significance of the cells is a matter of some importance in the interpretation of the observations in the various infantile disorders in which they are found.

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12. Wohlwill, F.: Zur Frage der sogenannten Encephalitis congenita (Virchow), Ztschr. f. d. ges. Neurol. u. Psychiat. **68**:384, 1921.

13. Ceelen, W.: Ueber Gehirnbefunde bei Neugeborenen und Säuglingen, Virchows Arch. f. path. Anat. **227**:152, 1919.

14. Schwartz, P.: Erkrankungen des Zentralnervensystems nach traumatischer Geburtsschädigung, Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:263, 1924.

Ranke looked on them as an indication of retarded development of the brain, and found the foci in cases of congenital syphilis, in one case of porencephaly in a child aged 1 year, in a case of microphthalmia and in a case of status corticis verrucosus deformis. With this view Wohlwill essentially agreed. He found them in the brain of a congenitally syphilitic child, aged 10 months, and expressed the belief that syphilis plays a rôle in their persistence. Schwartz,[14] too, expressed the opinion that the cells represent an evidence of retarded cerebral development. Ceelen, however, was much impressed with the constancy of the subependymal collections in encephalitis congenita of Virchow and came to the conclusion that they were inflammatory in nature. He expressed the belief that the cells within the centers are of two types, astrocytes and lymphocytes and plasma cells. He did not think that the foci around the vessels were so clearly inflammatory in nature, the cells consisting either of elements from the lymphatic system or of glia cells. With this view, however, Ranke and Wohlwill did not agree. The former believed that most of the cells are probably spongioblasts with possibly some neuroblasts. Wohlwill found some neuroblasts in his foci, though he was unable to demonstrate intracellular fibrils within their cytoplasm.

Following the conceptions of Ranke and Wohlwill, the foci in my case of an infant aged 4 months are definitely pathologic in import, having persisted some time beyond the normal limit. All the brains of normal infants which I examined showed scattered small foci in the periventricular region, but in far smaller number than in my case. Here were not only numerous foci in the white matter and around the ventricles, but also in large concentrated swarms which filled an entire low power field. As in Schwartz' case, most of the foci were in the frontal area of the brain. No evidence of cells of an inflammatory nature was found either in the perivascular or in the intramedullary foci. Lymphocytes and plasma cells were entirely lacking. The cells, as was pointed out by Ranke, correspond to the matrix cells of the embryo. A careful examination of the perivascular and subependymal foci was made to differentiate if possible, the type of embryonic cell which they represent. The nuclei, save for a slight variation in shape, were uniformly similar, and in no instance could a differentiation be made between primitive spongioblasts and neuroblasts. The morphologic structure of the cells seems to indicate that they are entirely of one sort, probably spongioblasts. This was all the more convincingly brought home by the structure of the periventricular region, which consisted of a layer of ciliated ependymal cells, below which were numerous loosely arranged cells also obviously ependymal and in some areas arranged very clearly in a syncytium. In this loosely arranged net could be seen scattered cells similar to those within the foci, and close

by, similar cells in groups such as have already been described. The impression to be gained, therefore, is that these cells are probably very closely allied to the ependymal cells and probably represent immature ependymal spongioblasts. That they still serve as centers of growth—though to what extent it is hard to say—is seen by the fact that mitoses can occasionally be seen within a focus.

Cortical Focus.—A large focus (fig. 5), similar in all respects to those in the white matter, was found in the parolfactory cortex. This focus penetrated diffusely into the cortical substance which was architecturally disturbed in consequence. In the midst of it lay a small ependymal-lined pouch. Davidoff [15] reported a similar focus in exactly the same region in one of his cases of mongolian idiocy. In his case he could trace the pouch back to the ventricle, but a study of serial sections in my case failed to reveal a similar connection. It seems probable, as Davidoff pointed out, that the pouch is a rest of the ventricular horn. Hochstetter [16] showed that the ventriculus olfactorius runs in the rhinencephalon and stretches posteriorly for some distance, bending basally to get into the free portion of the rhinencephalon and then proceeding frontally. He did not mention it after the 87 mm. stage. A similar canal is found posteriorly in the cerebellar anlage, seen first as the sulcus longitudinalis internus cerebelli; later, due to the growth of the lateral parts of the cerebellum, it produces an ependymal-lined canal which fuses at both ends with the fourth ventricle, and finally disappears at the 105 mm. stage. Yaskin [17] studied these pockets, one of which he found in a 210 mm. embryo, and pointed out their importance in the production of malformations and brain tumors. The ependymal pouch in my case is undoubtedly a rest of the ventriculus olfactorius, differing, however, from the normal in that it is wholly within the cortex. Other similar pouches were encountered in the white matter of the rhinencephalon and in the subependymal area.

Ganglion Cells and Astrocytes in the White Matter.—The abundance of ganglion cells in the white matter (figs. 6 and 7) is striking. This is not uncommon in normal infants, and is frequently found in the brains of idiots. In the normal infants' brains which I studied, ganglion cells were present but not in great numbers. In this case, they were extremely numerous, not only in the centrum ovale but also in the subcortical white matter. Their arrangement produced a striking effect,

15. Davidoff, L. M.: The Brain in Mongolian Idiocy, Arch. Neurol. & Psychiat. **21**:1229 (Dec.) 1928.

16. Hochstetter, F.: Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns, Vienna, Franz Deuticke, 1929, part 2.

17. Yaskin, J. C.: Ueber Entwicklungsanomalien bei Kleinhirnembryonen als Grundlage pathologischer Bildungen, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **31**:13 (May) 1929.

as of ganglion cells radiating from the deeper white matter to the cortex on which they seemed to be concentrating. According to His' view, this is exactly what they do. His looked on these cells as neuroblasts wandering from the matrix to the cortex. Ranke, however, looked on them simply as nerve cells within the white matter, due to the fact that among them are many fairly well matured ganglion cells which are probably fixed in the white matter. In a case of status corticis verrucosus deformis, Ranke also described the radiating arrangement of these cells. The fate of these cells after birth is totally unclear. They are unquestionably present at and after birth, as study in my normal cases showed, but their eventual fate is still obscure.

A further evidence of immaturity on the part of the brain substance is given by the astrocytes within the white matter (figs. 8 and 9). These are not adult, fibrous astrocytes, but correspond to what Ramón y Cajal [18] described as the juvenile type of neuroglia, which is found in the cat and dog of from 15 days to 2 months. This type of neuroglia is characterized by the relative poverty of expansions, by the great robustness of the sucker foot, by the relative abundance of undifferentiated somatic protoplasm and above all by the tangential position of the nucleus. These can be seen clearly in figure 9. The expansions of this young type of neuroglia are very fine and slender, and in contrast to the sweeping processes of the adult cell are short and crooked. In most of the astrocytes, the fibers of Ranvier-Weigert have not yet been laid down, but in some cells they can be seen already appearing in the sucker process. Isogenic forms are fairly frequent, and amitotic division is occasionally evident. These immature astrocytes are of no great significance in themselves, save that they demonstrate still further the general immature state of the entire brain in this case.

Giant Cells.—The large focus of giant cells at the frontal pole of the lateral ventricle is difficult to explain. In the normal infant's brain, scattered giant cells may be found under the ependyma but nowhere in foci similar to that shown in figure 13. This region of the brain was studied in serial sections, whereby these giant cells could be seen to stream out from the pole of the ventricle in an elongated focus, decreasing gradually in size. From this area they could be followed under the ependyma where they appeared as isolated cells, more numerous in some areas than in others, but still regularly present under the ependymal lining. Their presence in the normal brain suggests that these cells serve a definite function. They are, without much question, astrocytic multinucleated giant cells. It is possible that they may represent a multinuclear stage in the development of neuroglia, but I

18. Ramón y Cajal, S.: Contribucion al conocimiento de la neuroglia del cerebro humano, Trab. d. lab. de invest. biol. Univ. de Madrid **11**:255, 1914.

have no evidence on which to make this assumption. Minot [19] reported a multinuclear stage in the development of neuroblasts in fishes, but no such stage in the formation of astrocytes from spongioblasts has as yet been demonstrated. This assumption is therefore improbable. On the other hand, these cells may represent atypical forms of astrocytes which have been frustrated in their normal act of division. The formation of such astrocytic giant cells was studied in brain tumors by me.[20] I showed that they result from an incomplete division of astroblasts. What function these multinucleated astrocytes subserve in the subependymal region in the infant's brain cannot yet be answered with certainty.

Arteriosclerosis.—In one vessel in the pia there was found definite evidence of arteriosclerosis (figs. 17 and 18). This appeared as a small area of intimal proliferation, staining with a metachromatic tint with toluidine blue, and with an intact elastic membrane. No similar vessel changes were found anywhere else in the brain. Reports of calcification of vessels in infants' brains are not frequent. Herzog [21] reported this condition in a child, aged 7, who had died of carbon monoxide poisoning. Parrot [22] found it in a child aged 7 days, and Obersteiner [23] also found it in an infant. Schmincke [24] found calcified vessels in the brain of a child aged 9 months who had died of encephalitis congenita of Virchow, and attributed the vascular change to the toxic influence which produced the generalized cerebral damage.

SUMMARY

In the three cases that I have reported there were certain clinical and pathologic features of outstanding interest. All three cases presented clinical pictures of Little's disease with subnormal mentality, hyperkinesias, choreo-athetotic movements and epileptiform convulsions, with hypertonicity of the musculature and at times opisthotonos. The patients were aged 4 months, 8 months and 19 years. The anatomic substratum in each case consisted of a marked demyelinization of the cortex, due probably to a failure of development, and a similar though less

19. Minot, C. S.: Human Embryology, New York, William Wood & Company, 1892.

20. Alpers, B. J.: The Origin and Development of Giant Cells in Gliomas, Arch. Neurol. & Psychiat. **25**:281 (Feb.) 1931.

21. Herzog: München. med. Wchnschr. **22**:558, 1920.

22. Parrot, quoted by Schmincke, A.: Ztschr. f. d. ges. Neurol. u. Psychiat. **60**:290, 1920.

23. Obersteiner, H.: Anleitung beim Studium des Baues der nervösen Zentralorgane im gesunden und kranken Zustände, Vienna, Franz Deuticke, 1912.

24. Schmincke, A.: Encephalitis interstitialis Virchow mit Gliose und Verkalkung, Ztschr. f. d. ges. Neurol. u. Psychiat. **60**:290, 1920.

marked absence of fibers in the basal ganglia. The cortex showed a diffuse loss of ganglion cells in the third lamina. The microscopic examination in the three cases revealed, in my case, areas of incomplete necrosis scattered diffusely throughout the brain. In the case of Somoza the process was more advanced, and in the case of Freedom it was still more advanced. Though the three cases showed different cell pictures, I am inclined to look on them as different stages in the same process, rather than as three different types of reaction. In only one case, that of Somoza, could a definite etiology be adduced. In this case asphyxia was an important factor. In the other two cases a toxic process was probably operative.

The lesions described are confined almost entirely to the gray matter, in direct contradistinction to the pathology in diffuse sclerosis, which is largely confined to the white substance.

TUMOR OF THE BRAIN WITH DISTURBANCE IN TEMPERATURE REGULATION

THE HYPOTHALAMUS AND THE AREA ABOUT THE THIRD VENTRICLE AS A POSSIBLE SITE FOR A HEAT-REGULATING CENTER

REPORT OF THREE CASES *

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The regulation of body temperature in the warm-blooded animal is an old biologic problem. The physiologist has come to recognize in this mechanism a coordinated reflex act, which maintains a level body temperature in the normal animal by balancing the production with the elimination of heat. Such a delicately adjusted reflex mechanism is thought to be governed by a centralized nervous structure, and evidence is accumulating in favor of the existence of a subdivision in the brain that serves as a heat-regulating center. However, the exact site of this center is still in doubt. Many efforts have been made to localize it; many experiments have been performed, but as yet no conclusive results have been obtained establishing the exact location of such a center.

Among the several cerebral areas that are thought to contain a heat-regulating center is the corpus striatum. Aronson and Sachs [1] produced experimentally a rise in temperature in animals by injuring the corpus striatum with a blunt instrument. To control this experiment they converted their instrument into an electrode. The initial rise of temperature provoked by the stab wound in the corpus striatum was allowed first to subside; two days after the initial operation an electric current was passed through the instrument, and again a rise in temperature was obtained.

Barbour,[2] repeating the experiment of Aronson and Sachs, introduced into the corpus striatum an instrument so constructed that its

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1. Aronson, E., and Sachs, J.: Beziehungen des Gehirns zur Körperwärme, Arch. f. d. ges. Physiol. **37**:232, 1885.

2. Barbour, H. G.: Die Wirkung unmittelbarer Erwärmung und Abkühlung der Wärmezenter auf die Körpertemperatur, Arch. f. exper. Path. u. Pharmakol. **70**:1, 1912.

temperature could be altered. When the temperature in this instrument was raised the body temperature fell, and when the instrument was cooled the body temperature rose. Their observations led them to conclude that the corpus striatum contains a nucleus that is responsible for heat regulation.

Jacoby and Roemer [3] found that an injury to the ventricular wall or penetration into the lateral ventricles is essential for the production of a more or less decided elevation of temperature. They were inclined to assume that the implication of the choroid plexus may play an important rôle in the production of hyperthermia.

Ott [4] was the first to observe that it is essential for obtaining an elevation of temperature to reach the tuber cinereum in puncturing the thalamus. In another contribution,[5] basing his views on the results of sixteen experiments on rabbits, he advanced the idea that the tuber cinereum contains a thermal and respiratory center and that polypnea and thermotaxis are due to a disturbed function of this center.

Isenschmidt and Krehl [6] found that heat regulation may be preserved even after the extirpation of the cerebral hemispheres, including the corpus striatum, but that with the removal of the interbrain the animal is deprived of the heat-regulating mechanism and reverts to the condition of a cold-blooded animal. They concluded that the essential heat-regulating structures are situated in the ventromedian parts of the caudal end of the diencephalon. Complete vertical section of the brain between the thalamus and the anterior quadrigeminal body, leading to loss of the heat-regulating function, served as further proof that the subthalamic region contains structures essential for the maintenance of a balanced body temperature.

Isenschmidt and Schnitzler [7] were also able to demonstrate experimentally in the rabbit that the tuber cinereum is the important part of the diencephalon which serves as the central organ for heat regulation.

Leschke [8] destroyed the medial portion of the subthalamic region in rabbits and caused the loss of the heat-regulating function.

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3. Jacoby, C., and Roemer, C.: Beitrag zur Erklärung der Wärmestichyperthermie, Arch. f. exper. Path. u. Pharmakol. **70**:149, 1912.

4. Ott, Isaac: Interbrain, Its Relation to Thermotaxis, Polypnoea, Vasodilatation and Convulsive Action, J. Nerv. & Ment. Dis. **18**:433, 1891.

5. Ott, Isaac: Function of Tuber Cinereum, J. Nerv. & Ment. Dis. **18**:431, 1891.

6. Isenschmidt, R., and Krehl, L.: Ueber den Einfluss des Gehirns auf die Wärmeregulation, Arch. f. exper. Path. u. Pharmakol. **70**:1091, 1912.

7. Isenschmidt, R., and Schnitzler, W.: Beitrag zur Lokalisation des Wärmeregulation vorstehenden Zentralapparatus im Zwischenhirn, Arch. f. exper. Path. u. Pharmakol. **76**:202, 1914.

8. Leschke, Erich: Ueber den Einfluss des Zwischenhirns auf die Wärmeregulation, Ztschr. f. exper. Path. u. Therap. **14**:167, 1913.

Unfortunately there are few clinical and pathologic observations to support these conceptions. On the other hand, ample clinical material indicates that the hypothalamus and adjacent parts of the diencephalon contain nuclei that regulate many of the vegetative functions, such as centers for carbohydrate metabolism, water elimination, protein metabolism, fat distribution, fat consumption, vasomotor function and the secretory activity of sweat and other glands. If it is recognized that the production of heat is dependent on the carbohydrate, protein and fat metabolism (Raab [9]), and that elimination of heat is procured through vasodilatation in the skin, sweat secretion and elimination of fluids (urine and sweat), it becomes obvious that a heat-regulating mechanism, if it exists, is likely to be located near centers that control functions essential for the maintenance of a balance between production and elimination of heat. This would seem to add weight to the belief that such a center has its location in or near the subthalamus.

This brief comment, of course, does not exhaust all the data favoring the hypothalamus as the seat of a heat-regulating center, nor does it include the several objections raised against the existence of a central organ for the regulation of heat (Tiegerstadt,[10] Sachs [11]). The problem is more thoroughly treated in modern monographs on the autonomic nervous system, in which the physiologic significance of the diencephalon is fully recognized and discussed in detail. In this contribution, our aim is to add a few observations based on the study of clinical and anatomic material, which seemed to offer support to the views favoring the existence of a thermal center in the diencephalon.

REPORT OF CASES

CASE 1.—*History.*—J. S., a woman, aged 52, married and with two children, consulted one of us (I. S.) on June 18, 1928. She had been operated on ten years before for peritonitis. Two years later, a second operation was performed for adhesions resulting from the first operation. Roentgen treatment was given and caused the menopause. Before and after the second operation, bladder control was poor. Following the second operation, the patient was weak and unable to walk for about three months. Several teeth were extracted at this time. For three months prior to admission to the hospital it had been noticed that the memory had become defective. The patient felt weak and wanted to sleep continuously. She would wander away from the hotel at which she resided and would be unable to find her way back; also she could not recall the name of the hotel. In conversation, she would become confused and lose the trend of her thought. One month later, she began to realize that her mind was not functioning

9. Raab, W.: Wärmeregulation und Fettstowechsel, Ztschr. f. d. ges. exper. Med. **53**:317, 1926.

10. Tiegerstadt, R.: Lehrbuch der Physiologie des Menschen, Leipzig, S. Herzel, 1919, vol. 1, p. 625.

11. Sachs, Ernest: On the Relation of the Optic Thalamus to Respiration, Circulation, Temperature and the Spleen, J. Exper. Med. **14**:408, 1911.

properly. She complained a great deal of headache. Shortly afterward she became jaundiced for a short time. The family physician saw her then and thought that there had been an infection of the gallbladder. She did not remain under continuous observation.

About this time, she consulted a neurologist, who found that the left knee jerk was more active than the right, that there was a Babinski sign on the left side, that there was stiffness at the left ankle, and that she dragged her left leg a little. These signs were not found at a subsequent examination a few days later. No diagnosis was made. It was then discovered that the patient had a temperature ranging as high as 102 F. (fig. 1), and on June 28, 1928, she was admitted to Mount Sinai Hospital.

Examination and Course.—Repeated examinations demonstrated no signs referable to the central nervous system. A general physical examination gave negative results. Examination of the cerebrospinal fluid also gave negative results. The patient remained in bed in a somnolent condition. She could be aroused to take food. She would converse for a short period; at the beginning the answers would

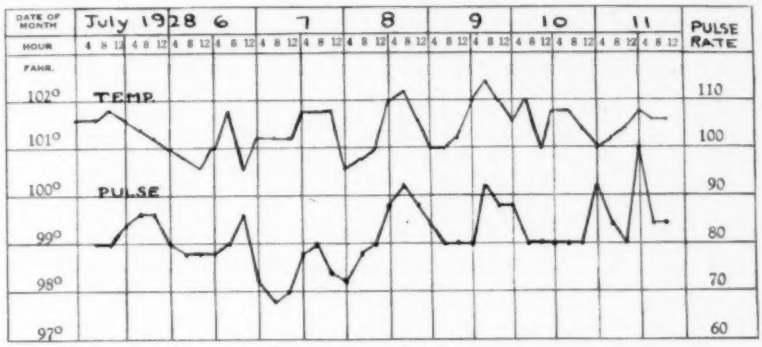

Fig. 1 (case 1).—Temperature and pulse charted during the patient's second week (July 5 to July 11) in the hospital. Except for the period during which the patient received foreign-protein therapy, the temperature continued a similar course.

be rational, but then she would lapse into a condition in which she would become at times incoherent or answer in an irrelevant manner. She was oriented, but the memory defect was pronounced and gradually became more marked.

On July 21, 1928, in trying to find a cause for the high temperature, which was constantly between 100.4 and 102 F., a cystoscopy was performed, and both kidneys were catheterized. The urine from the catheter seemed slightly bile-tinged, although there was no jaundice at this time. The urine was also turbid, and bacteria were found in the specimens. Cultures revealed *Bacillus coli.* An agglutination test for typhoid and paratyphoid organisms yielded a negative result. Blood cultures likewise were negative. At times, the patient was incontinent. At one time for a period of about twelve hours the four extremities assumed a position of extreme flexion. The gallbladder was examined by means of the x-rays, with negative results. At the same time the chest was examined with the x-rays, and a malignant growth was excluded.

On July 13, typhoid vaccine was administered intravenously for the purpose of seeing the effect of nonspecific protein therapy. There was a slight rise in temperature. On July 14, the vaccination was repeated, and the temperature rose to 104. Again on July 16, the temperature rose to 104. It remained at this level without any recession until death.

On July 27, another lumbar puncture was done; it was reported by the laboratory that an acid-fast beaded bacillus was found. However, we thought that this had no bearing on the case, for clinically the patient did not present the picture of tuberculous meningitis (no headache and no meningeal signs).

The patient continued to lose ground, the temperature rising higher and higher; on the day before death a consultant advised a laparotomy, believing that he felt a mass in the region of the gallbladder. It was done under local anesthesia, but no abnormality was found. The patient died on the following day.

At all times the patient took ample nourishment, both liquid and soft foods, although the nurse had to arouse her and force the feeding because it was difficult to induce her to swallow food.

The results of the examinations of the blood were as follows: June 28, hemoglobin, 100 per cent; red cells, 4,500,000; white cells, 10,500; polymorphonuclears, 84 per cent; lymphocytes, 16 per cent. July 18, hemoglobin, 85 per cent; red cells, 4,320,000; white cells, 9,000; polymorphonuclears, 68 per cent; lymphocytes, 32 per cent. July 24, white cells, 11,250; polymorphonuclears, 84 per cent; lymphocytes, 16 per cent. July 30, hemoglobin, 80 per cent; white cells, 19,500; polymorphonuclears, 90 per cent; lymphocytes, 10 per cent.

Diagnosis.—During the illness the patient was seen by various consultants. The diagnoses of pyelonephritis, abscesses in the kidneys, encephalitis and inflammation of the gallbladder were made. These diagnoses were not acceptable, because they did not accord with the clinical picture presented nor were they substantiated by any of the diagnostic methods. If autopsy had not revealed the presence of multiple tumors of the brain, the diagnostic problem would have remained unsolved.

Necropsy.—The brain was rather small; the gyri were somewhat atrophic. On section, a nodule about the size of a kidney bean (fig. 2*A*) was seen protruding from the ependymal wall into the anterior horn of the left lateral ventricle. It was continuous with a mass infiltrating the septum pellucidum and was of firm consistency. Another coronal section on a level with the optic chiasma displayed a tumor mass which involved the body of the corpus callosum and measured about 1.5 cm. in its long axis. Below this tumor was another tumor in the right hypothalamic region, directly above the right optic tract (fig. 2*B*). This tumor was grayish and also of firm consistency; it extended backward for a distance of about 1 cm. Because of the infiltrating character of the tumor, gross photography did not bring out its actual size and limitation. The region of the third ventricle, including its floor, was removed in toto and cut serially. In stained preparations it was possible to map out the extent of the main tumor. Figures 3, 4, 5 and 6 show that the lateral walls of the third ventricle and almost the entire floor were invaded by the neoplasm. The growth seemed to be most prominent in the region of the tuber cinereum (fig. 4) and of the massa intermedia with the areas surrounding it (fig. 5).

It was impossible to map out any of the various nuclei in the floor and walls of the third ventricle, because of the massive invasion by neoplastic tissue of the zones occupied by these nuclei.

Sections of the invaded areas showed a densely cellular neoplastic process with large areas of degeneration. There were vast numbers of large multinucleated giant cells, many of which were undergoing mitosis (figs. 7 and 8). Throughout the tumor the cells were frequently arrayed in rosets. The histologic character

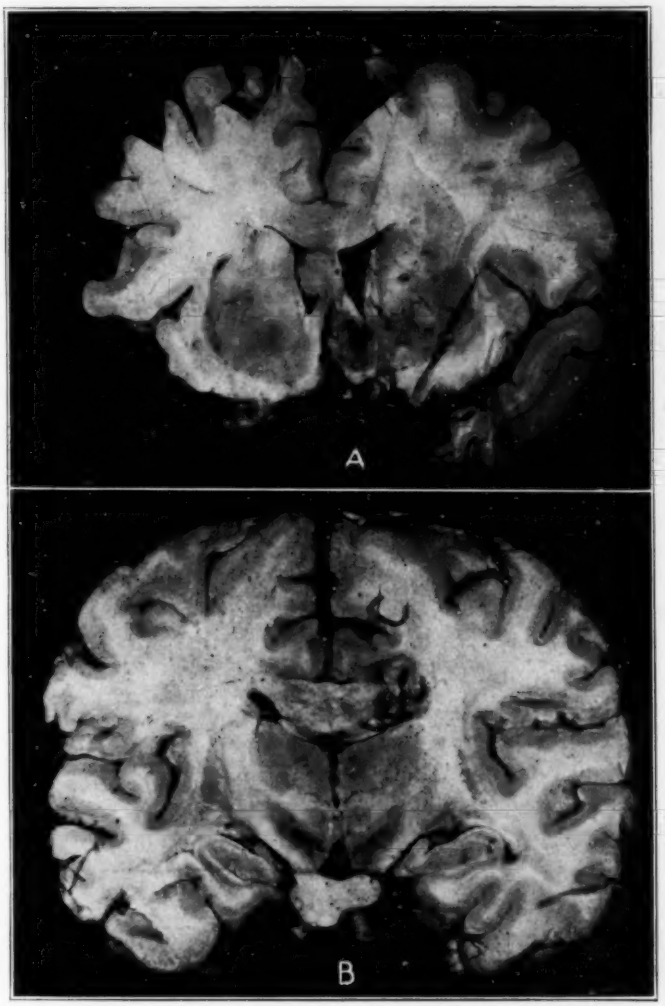

Fig. 2 (case 1).—Photograph showing the location of tumor nodules.

of the tumor will be described elsewhere. Its general characteristics were those of spongioblastoma [12] (fig. 12).

12. Globus, J. H., and Strauss, I.: Spongioblastoma Multiforme (A Primary Malignant Form of the Brain Neoplasm), Arch. Neurol. & Psychiat. **14**:139 (Aug.) 1925.

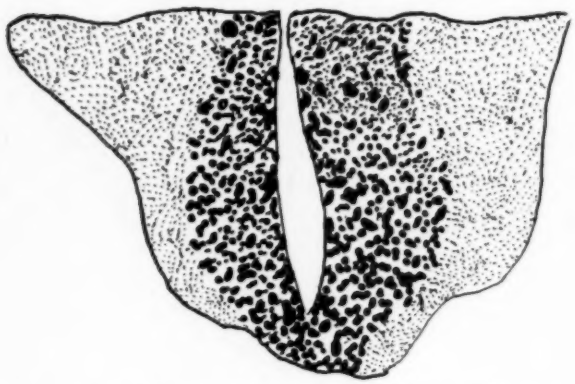

Fig. 3 (case 1).—Drawing traced from a photomicrograph of a section from the anterior extremity of the tuber cinereum, showing the extent of the neoplastic process.

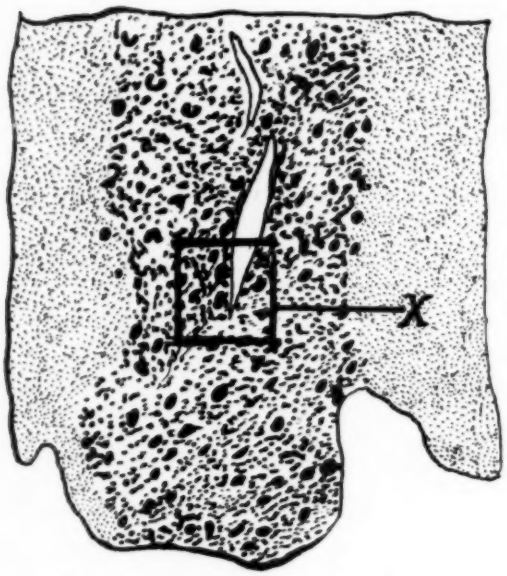

Fig. 4 (case 1).—Drawing traced from a photomicrograph of a section of the diencephalon at the level in the midportion of the tuber cinereum, showing the extent of neoplastic invasion. The small square *X* is a field shown under higher magnification in figure 7.

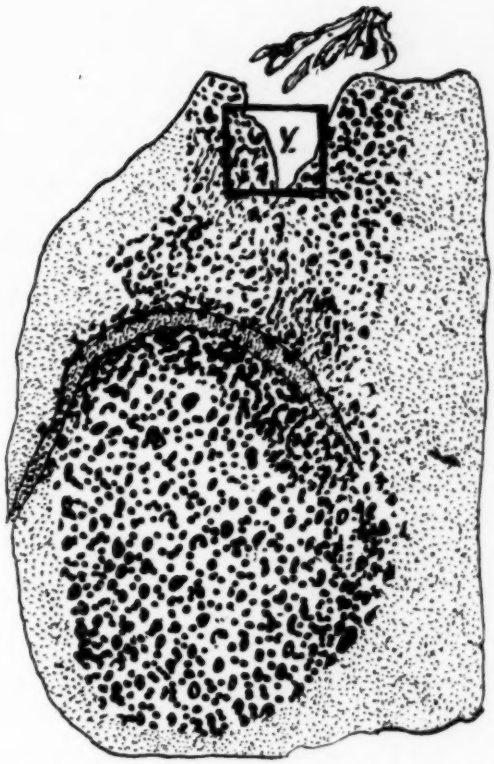

Fig. 5 (case 1).—Drawing traced from a photomicrograph of a section of the diencephalon taken at the level of the massa intermedia. The small square *Y* is shown under higher magnification in figure 8.

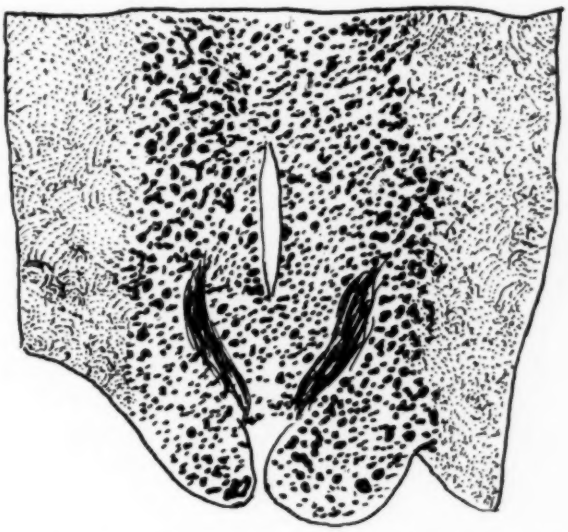

Fig. 6 (case 1).—Drawing traced from a photomicrograph of a section of the diencephalon at the level of the corpora mamillaria, showing the extent of the neoplastic invasion.

Case 2.—*History.*[13]—P. K., a man, aged 62, about two months prior to admission to the hospital began to manifest changes in personality. He would lapse easily into sleep. When alert, he was unusually loquacious and somewhat incoherent. During the same length of time he had complained of intense headache.

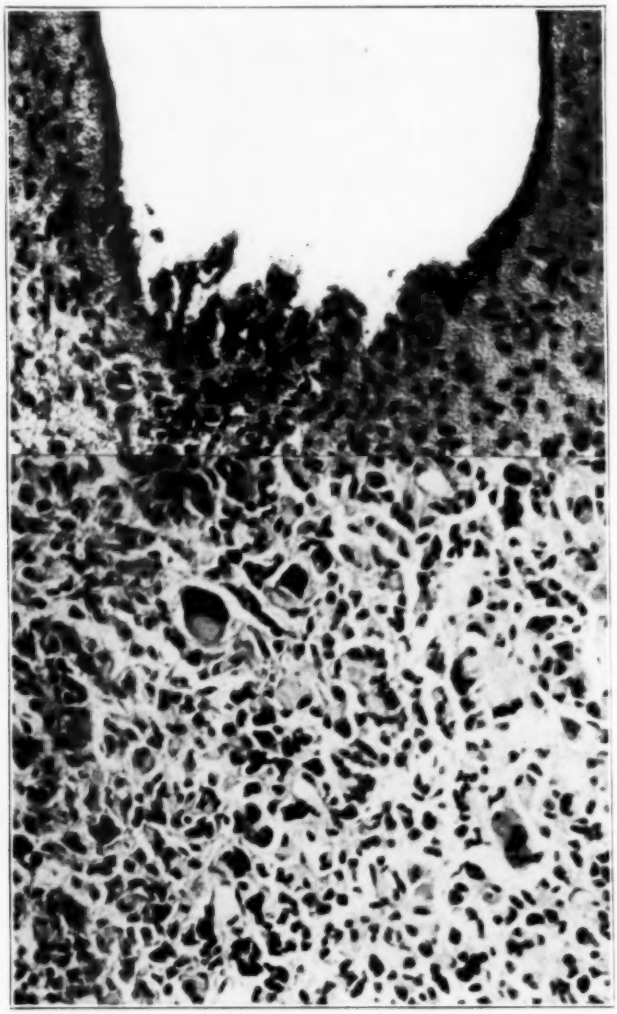

Fig. 7 (case 1).—Photomicrograph of sections of the tumor, taken from the region of the thalamus marked in drawing 4 by *X*.

Examination.—The objective neurologic signs were few. They included: temporal anomia, slight right hemiparesis and increased deep reflexes on the right side.

13. The patient was under the care of Dr. E. D. Friedman, who plans to report the case in detail elsewhere. Only the salient points in the history are included.

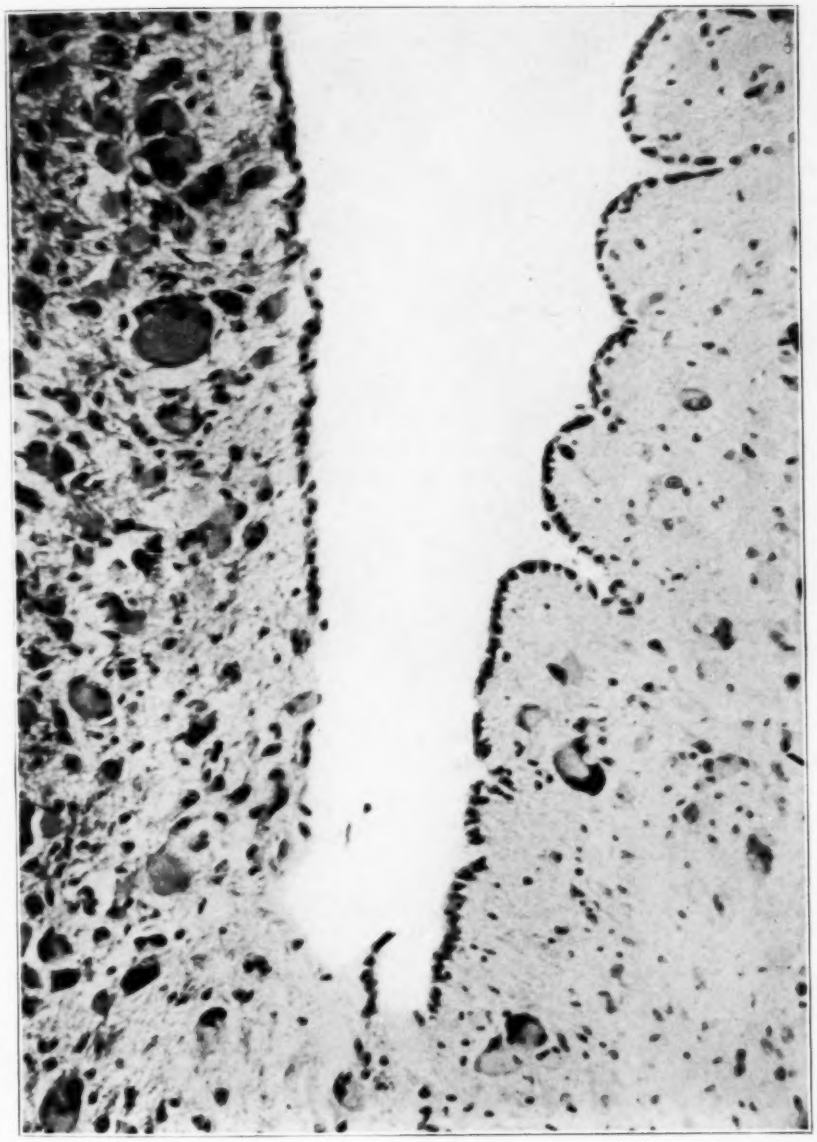

Fig. 8.—Photomicrograph of a section of the tumor taken from the region of the third ventricle marked in drawing 5 by *Y*.

Course.—Among the striking features characterizing the clinical course during the six and a half weeks that the patient was in the hospital was the elevation of temperature; it was observed from the first day in the hospital (it may have been present before admission) and continued until the fatal issue. The temperature fluctuated between 100 and 103 F. (fig. 9). No cause for the rise in temperature could be found. Examination of the cerebrospinal fluid and many other biologic tests (Widal test and blood cultures), as well as roentgen examination of the chest, excluded an inflammatory or malignant disease.

Finally, an exploratory craniotomy was resorted to. A left frontotemporoparietal flap was turned down. A yellow cortex in the region of the temporal lobe was revealed. It was thought to indicate the presence of a deep-seated tumor causing secondary degeneration. Following the operation, the patient declined rapidly and died six and a half weeks after admission to the hospital.

Necropsy.—On section of the brain, a large tumor was found in the region of the right thalamus and hypothalamus (fig. 10). It invaded these structures in their

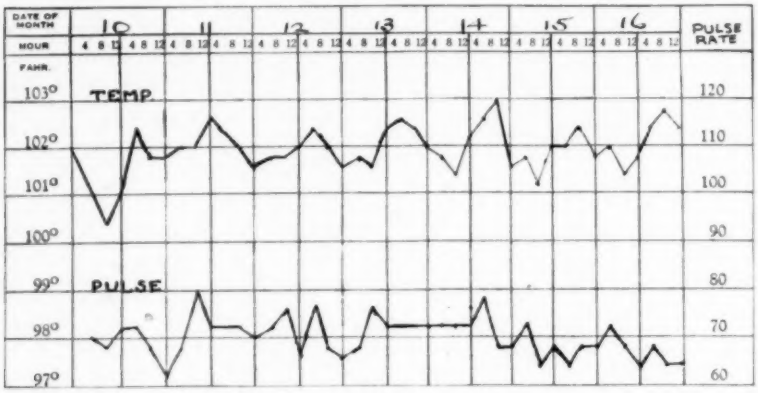

Fig. 9 (case 2).—Temperature and pulse charted during the patient's second week in the hospital. The temperature curve shown, with but slight variations in degree, characterized the entire clinical course.

ventral and mesial parts, extending from the walls of the third ventricle as far as the tuber cinereum below and as high as the taeniae thalami above. Laterally, the tumor spread as far as the internal capsule, narrowing somewhat in its upper part. Its anterior extremity was on a line with the genu of the corpus callosum. Posteriorly, it reached the anterior extremity of the red nucleus. Another tumor was found in the third temporal convolution of the left hemisphere about 2 cm. posterior to the temporal lobe. It measured about 1 cm. in diameter. It was nodular and well demarcated from the adjacent tissue. Both tumors were granular and of hard consistency. The larger mass showed invasive tendencies, while the smaller mass was discretely outlined and gave the impression of being encapsulated. In this case again, gross study of the tumor did not disclose the entire extent of the tumor invasion. In figures 11 and 12 it will be noted that though the tumor is predominantly in the right wall of the third ventricle, occupying a large zone in the thalamus and subthalamus, the subependymal zone of the third ventricle of the left wall is also involved, but to a much less degree.

The histology of this tumor is strikingly similar to that in case 1, except that it shows more extensive areas of degeneration (fig. 13). The neoplasm is gliogenous, with many giant cells and roset formations (spongioblastoma).

CASE 3.—*History.*—L. B., a woman, aged 57, began to show changes in personality during the year preceding admission to the hospital. She became more

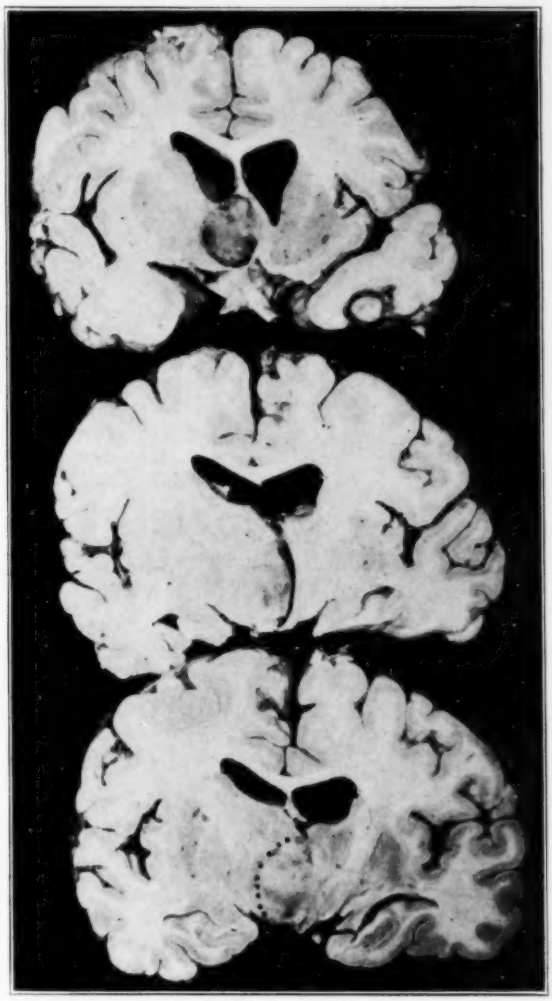

Fig. 10 (case 2).—Photographs illustrating the location of the tumor. It is best seen in the uppermost photograph, where the nodule in the left temporal lobe is also well shown.

forgetful, irritable, somewhat euphoric and voracious. During the last three months she slept much during the day and ate constantly during waking moments.

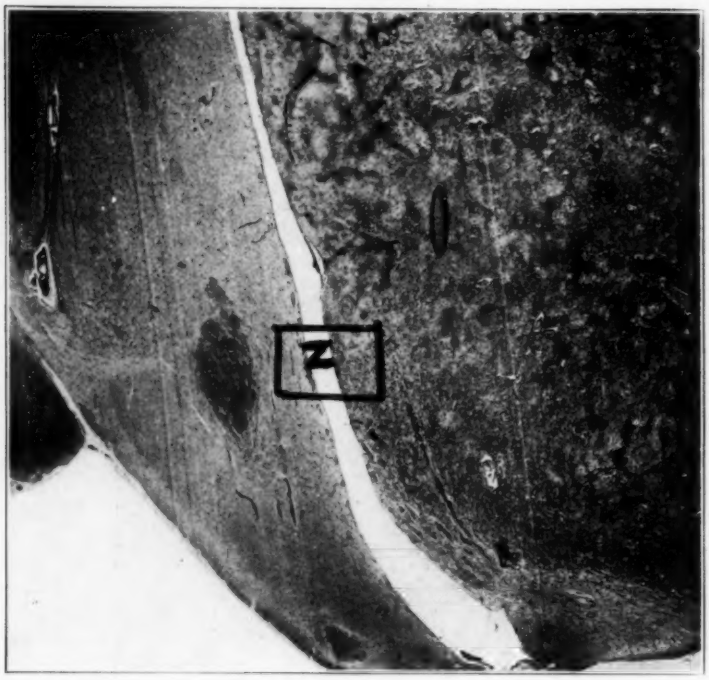

Fig. 11 (case 2).—Photomicrograph of a section of the diencephalon, showing the widespread neoplastic process in the right thalamus. The small square *Z* indicates the area from which the section shown in figure 12 was taken.

Fig. 12 (case 2).—Higher magnification of the field marked by the square *Z* in figure 11, to show the tumor invasion of both walls of the third ventricle.

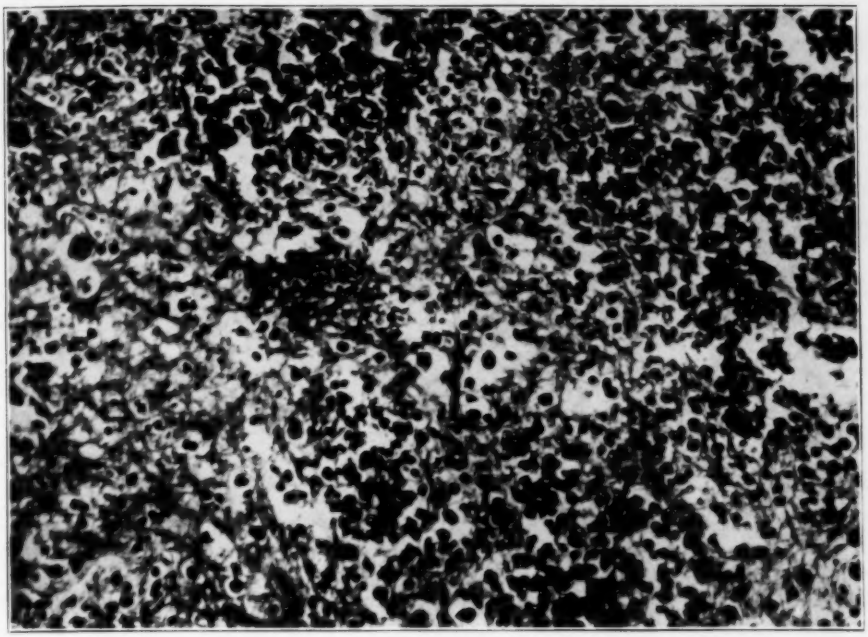

Fig. 13 (case 2).—Photomicrograph showing the histologic character of the tumor.

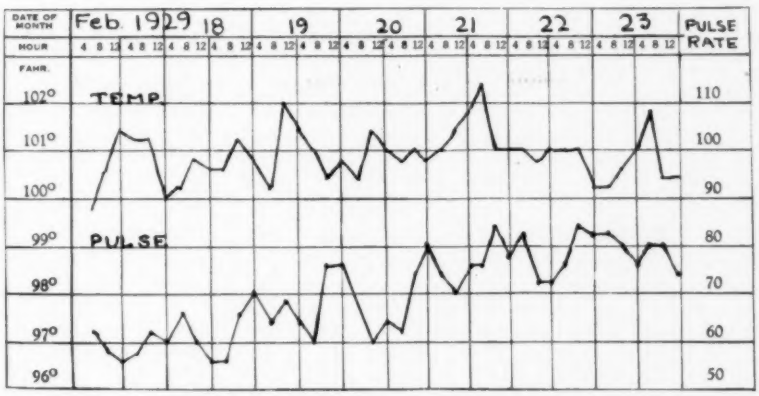

Fig. 14 (case 3).—Temperature and pulse charted during the patient's second week (Feb. 17 to Feb. 23) in the hospital. Note the occurrence of an extremely slow pulse.

Examination.—The patient was dull and apathetic, sleeping most of the time. She was poorly oriented. Memory was markedly impaired. She showed few neurologic signs: irregularity and inequality of the pupils, slight weakness of the right side of the face, deviation of the tongue to the right and depressed deep reflexes.

Course.—Because of the scarcity of objective observations, the slowly progressive clinical course, the peculiar mental pictures and the vegetative disturbances, a diagnosis of tumor of the brain probably located in the floor of the third ventricle was made by one of us (J. H. G.). The elevation of temperature that marked the patient's stay in the hospital was not fully understood. From the day of admission until the day of discharge the patient had an irregular temperature, fluctuating between normal and 103 F. The rises and falls occurred with striking irregularity. In spite of the elevation of temperature, the pulse rate was extremely slow (fig. 14). The patient declined progressively. She was transferred to another hospital, where she died twenty-four hours later.

Necropsy.—The base of the brain, just behind the optic chiasm, presented an almond-shaped tumor, slightly granular on the surface and with a mottled bluish appearance. It was adherent laterally to the middle aspect of the optic tracts, and when the optic chiasm was elevated the prolongation of this tumor was seen beneath it, as though the mass extended from an area between the two lobes of the brain. It was adherent to the undersurface of the chiasm and the portions of the optic nerves most proximal to the chiasm. The tuber cinereum and mammillary bodies could not be distinguished, as the tumor emerged in this space. The optic tracts were pushed laterally by the growth, which extended posteriorly to the pons and posterolaterally to the cerebral peduncles. It did not encroach on either of the structures.

The histologic diagnosis recorded by Dr. L. Stevenson was glioma of the third ventricle attached to or arising from the optic chiasm.

SUMMARY AND CONCLUSIONS

Three unusual cases of tumor of the brain are described. Each of the three cases clinically presented difficult localizing problems and lacked convincing evidence of the presence of an expanding intracranial lesion. In one case (no. 3), the diagnosis of a tumor of the third ventricle was made during life on the basis of a slowly progressive course, a few objective signs of organic character and an alteration of personality. In case 1 a diagnosis of cerebral tumor was considered, but the lack of objective signs and the misleading febrile course, with memory defect and somnolence as the only neurologic manifestations, made it almost impossible to reach a definite diagnosis. Each of the three cases ran a febrile course, but an adequate explanation for the elevation of temperature was not advanced. In case 1, the febrile course, added to the apparent tenderness in the right hypochondrium, led to an exploration of the abdomen, with negative results. In case 2, after every other possible source for the fever had been excluded, a cerebral origin was considered, but its localizing value was not recognized. In each of the three cases, a neoplasm in the subthalamic region with

variable involvement of the hypothalamus and thalamus was found. Because of the invasive character of the tumor, no limitation to distinct nuclei could be established. Hence the only interpretation that may be drawn from our material is that a lesion (in our cases neoplastic) in the periventricular zone of the third ventricle and in the tuber cinereum caused a disturbance in the function of the heat-regulating mechanism.

ABSTRACT OF DISCUSSION

DR. CHARLES A. ELSBERG, New York: At the Neurological Institute, we are very much interested in the occurrence of fever in tumors of the brain unexplained by any other lesion. In the first place, all of us who operate have seen patients succumb with high fever. We all know and dread the occasional occurrence of high fever after operations in or near the hypothalamic region.

About six months ago, we had occasion to observe, at the Neurological Institute, a child with a tumor involving the floor of the third ventricle, who had an irregular fever for a considerable period. In our large series of tumors we found, in addition to this one, only three others, and all are of interest because of the location of the tumor in each instance, and because of what happened after the neoplasm was totally or partially removed. The first was a case of spongioblastoma multiforme in the left occipital lobe in a man who had irregular rises of temperature varying between 100 and 102 F. for at least one month before he was operated on. After the evacuation of cystic fluid and the partial removal of the tumor located well back in one occipital lobe, the signs of increased pressure from which he was suffering disappeared, and the temperature promptly fell to normal and remained normal up to the time of his discharge from the hospital. The tumor was far away from the hypothalamic region, although he had a fairly marked increase of intracranial pressure with considerable dilatation of the lateral and the third ventricles. The important fact is that the fever disappeared after a partial removal of the neoplasm and the reduction of the increased intracranial pressure.

The second case was one of fibrous astrocytoma in the left frontal lobe which may have extended down to or very near to the hypothalamic region. The tumor was excised in two stages. For several weeks—the period of observation of the patient in the hospital before he was operated on—he had a temperature that varied between 100.2 and 101.4 degrees. After the operation, with a reduction of the signs of increased intracranial pressure and disappearance of papilledema, the temperature dropped to normal and remained normal for a year—the period of observation since the operation.

The third patient was a child who had a cystic glioma, probably an astrocytoma, in the left cerebellar lobe. This child had, for a number of weeks before operation, temperatures as high as 101 degrees that could not be explained. After the operation there was a reduction of increased intracranial pressure and the temperature dropped to normal.

It is surprising that in so many patients with marked intracranial pressure over long periods, as in all obstructive lesions in the posterior fossa and those which involve the aqueduct and the third ventricle, fever of this kind is so very rare. Therefore much more work has to be done before we can conclude that the hypothalamus is the center or the only one for temperature regulation. The cases reported by Drs. Strauss and Globus are very instructive and interesting, but they are not conclusive as to the location or extent of areas in which lie cells that exercise control of the temperature of the body.

DR. SIMON P. KRAMER, Cincinnati: I wish to suggest that there is one class of tumors which never occurs in the cerebrospinal axis, but which is always accompanied by fever, and in fact the diagnosis is usually missed for that very reason. I am referring to hypernephromas. Then there is always the possibility

that what we call a tumor may be something else; a syphiloma and a tuberculoma at one time were called tumors.

DR. EMANUEL D. FRIEDMAN, New York: These cases are extremely interesting and instructive, because they fall in line with a great deal of experimental work in this field. It has long been known that striate puncture (or Striatumstich, of the Germans) gives rise to hyperthermia. Evidently lesions in this vicinity disturb the heat-regulating mechanism.

Jacobi and Roemer found that the introduction of mercury into the ventricles of the brain, especially in the region of the third ventricle, gave rise to hyperthermia. Some recent work by Bruman (1929) seems to bear out the original observations of Jacobi and Roemer. His conclusion is that the temperature center has its seat in the region of the tuber cinereum.

While in the cases presented by Drs. Strauss and Globus there were multiple lesions in the central nervous system, yet the lesion common to all of them was one in the wall of the third ventricle. We are therefore justified in assuming an etiologic relationship between the lesion so located and the incidence of hyperthermia, which would otherwise have to remain unexplained.

DR. ISRAEL STRAUSS, New York: The experimental evidence obtained, as Dr. Elsberg says, is in many respects inconsistent. Nevertheless, there is enough of value in it to indicate that in the region of the hypothalamus or the walls of the third ventricle there are some cells that influence temperature in the body. Whether they are the only centers regulating temperature no one knows, and probably they are not, because the brain axis, as we all know, has more than one center interfering with, or having something to do with, vital processes of the body.

The case of spongioblastoma in the occipital lobe which Dr. Elsberg has cited, and in which he thinks there was no involvement of the hypothalamus, has not as yet come to autopsy. He cannot tell from his operation whether or not that spongioblastoma reached farther inward and forward so as to involve the hypothalamus. Even though the temperature was relieved by the operation, that does not mean that the neoplasm could not have pressed on this sensitive region and produced an elevation of temperature which the operation removing that pressure caused to disappear.

It is interesting to note that in our three cases, particularly the first in which no objective neurologic signs were shown, there was no internal hydrocephalus. We report these cases because, as borne out by Dr. Elsberg's study of his numerous tumors of the brain, the occurrence of a persistent temperature of this degree over a long period of time is a most unusual syndrome in cerebral tumors.

THE BRAIN AND THE CEREBROSPINAL FLUID IN ACUTE ASEPTIC CEREBRAL EMBOLISM

AN EXPERIMENTAL AND PATHOLOGIC STUDY *

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AND
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It would seem that the pathology of cerebral embolism should be a settled subject. This may be true for the late stages of the process. Current textbooks on pathology and contemporary medical literature show, however, that the most acute phases of the process are not widely understood.

The purpose of this report is to point out that the pathologic reaction in the brain as a result of sudden infarction is the same as that which occurs with sudden destruction in other tissues of the body. Polymorphonuclear neutrophilic leukocytes infiltrate the involved area quickly. They reach the meninges, and in this early period can frequently be found in the cerebrospinal fluid. They are transient and disappear completely after a relatively short time.

Attention was first attracted to the polymorphonuclear leukocytic reaction, the result of cerebral embolism, in a study focused primarily on the acute degenerative changes which occurred in neuroglia. Interest in the reaction was greatly heightened when a patient demonstrated that the reaction had a clinical significance. A preoperative diagnosis had been made of a so-called weeping abscess of the brain. The history was necessarily incomplete. Two hundred and forty cells per cubic millimeter, 80 per cent of which were polymorphonuclear leukocytes, were present in the fluid twenty-four hours after hemiplegia and uncon-

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* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 10, 1930.

* The experimental work was carried out in Prof. A. O. Whipple's surgical department at the College of Physicians and Surgeons of Columbia University in New York.

* Prof. Walter Palmer gave us permission to cite the clinical histories of the three cases from the medical service at the Presbyterian Hospital in New York. Prof. J. O. Meakins gave us the data on the case from his service at the Royal Victoria Hospital, Montreal. Prof. J. W. Jobling permitted us to study and include the pathologic material from the cases from the Presbyterian Hospital.

sciousness had developed. There were no bacteria in the smears and cultures subsequently reported were negative. At the operation the exposed brain was gray and soft, and the specimen removed in a hollow brain needle showed not only the acute degenerative changes in neuroglia which we had encountered in experimental animals, but also the same polymorphonuclear leukocytic reaction. No bacteria could be stained in the sections.

The material on which this report is based has been gathered chiefly from animals in which aseptic cerebral emboli have been produced and from cases in human beings in which final and complete examination proved that cerebral infarctions were the result of noninfected emboli. One case is recorded in which the history and examination of the patient suggested that sudden embolism had occurred and showed polymorphonuclear neutrophilic leukocytes in the cerebrospinal fluid. This case is cited as illustrating our thesis, though necropsy was refused.

EXPERIMENTAL METHODS

Dogs were used in the experiments. Black silk suture material cut into fine bits and suspended in physiologic solution of sodium chloride, poppy seed, begonia seed, tobacco seed and paraffin melting at 45 C. were the various agents used for emboli. Of all these, the melted paraffin was most easily injected.

The materials to be used for emboli were sterilized in the autoclave under 17 pounds' pressure by the fractional method. The injections were carried out with strict aseptic technic. The animal's neck was widely shaved and prepared with 7 per cent iodine. Under ether anesthesia, the common carotid artery was exposed and the emboli were injected. When seeds were used, they were washed in by aspirating blood into the syringe containing them and then injecting. The paraffin, heated to its melting point, was poured into a warm syringe, the attached needle was held for a moment over an alcohol flame and a stream of paraffin started through the needle. Without allowing the flow of paraffin to stop, the needle was plunged into the artery. Thus any desired quantity of paraffin could be injected. In most instances it was necessary to tie the common carotid artery below the site of injection because of hemorrhage from the needle track. The incision in the neck was sutured in layers and covered with a narrow band of sterile cotton wool fastened to the neck with collodion.

The animals were allowed to survive the cerebral insult for variable periods up to seven days. Just before they were killed, a cisternal puncture was done. If no cerebrospinal fluid were obtainable for cytologic study by this method, an attempt was made to obtain it by ventricular puncture.

ANALYSIS OF MATERIAL

It was impossible to predict where the emboli would lodge. However, the signs resulting from the injection were constant in the animals included in this report. As the injections were being made, a change from quiet to stertorous breathing took place, and the pupil on the side of the injection became dilated. As the anesthesia passed, varying

degrees of paralysis of the contralateral limbs were evident. At times the animals were blind on one side. Often, infarction of the temporal muscle occurred. When 0.5 cc. of epinephrine (1:1,000) was injected into the jugular vein just before the injection of the emboli, infarction of the temporal muscle was never marked.

Of the animals in which cerebral emboli were produced and which are not included in this report, some died a few minutes after the emboli were produced. Many never recovered from the anesthesia. Still others, as the effect of the anesthesia wore off, had repeated convulsions. were very restless and died within a few hours. In these animals the emboli generally blocked the circle of Willis and many of its branches.

Two animals that lived and were studied are not included because gas bacilli were stained in the infarcted temporal muscle, though no organisms were discovered in the infarcted areas of the brain.

Unless an animal showed clinical evidence of damage of the brain it was not studied.

Twenty dogs showed clinical signs of cerebral embolism, and subsequent study proved them to be noninfected. They were killed: one eight and one-half hours after the operation, one at eighteen hours, six at twenty-four hours, one at thirty-eight hours, four at forty-four hours, one at forty-eight-hours, four at seventy-two hours, one at ninety-six hours and one at seven days.

OBSERVATIONS AT NECROPSY

Gross Examination.—In the cases included, areas of infarction were present only on the side on which the injection was made. Usually small branches of the middle cerebral artery, or at times the main trunk, were blocked. There was swelling of the infarcted hemisphere, slight in the earliest stage, very marked from the twenty-four hour period on. With this swelling the convolutions were flattened and the intergyral fissures were narrowed. The increase in intracranial tension had been so great in one animal that a part of the cerebellum was pushed down beneath the arch of the atlas, obliterating the cisterna magna and making it impossible to obtain cerebrospinal fluid here. This may have occurred in other instances in which cisternal punctures were unsuccessful.

On section, the normal cortical markings were altered. The gray matter in the softened area was widened. The normal sharp transition between gray and white matter was lost. On the slightest manipulation, the gray cortex separated from the white matter. Small hemorrhages were frequently present not only in the brain but also in the leptomeninges.

The areas of softening at times involved the basal ganglia, and at times the ependyma and its bordering nerve tissue were softened. As the length of time after the embolus had been produced increased, the outlines of the areas of softening became more and more sharp.

Microscopic Examination.—Blocks were taken from both normal and softened areas, fixed in Zenker's fluid and embedded in paraffin, and the sections were stained with eosin-methylene blue (methylthionine chloride, U. S. P.) hematoxylin and eosin and Gram's stain. Special fixatives and stains were used. Aside from

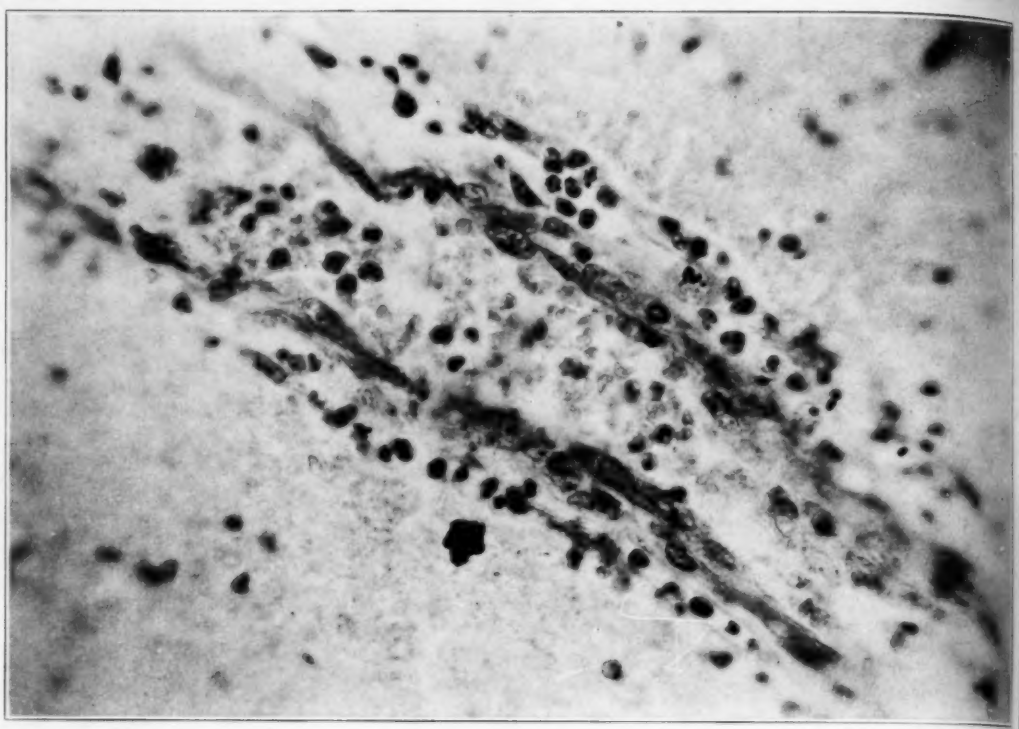

Fig. 1.—Polymorphonuclear neutrophilic leukocytes in the perivascular space of a cerebral vessel from the infarcted area (eight and one-half hours after the production of the embolism).

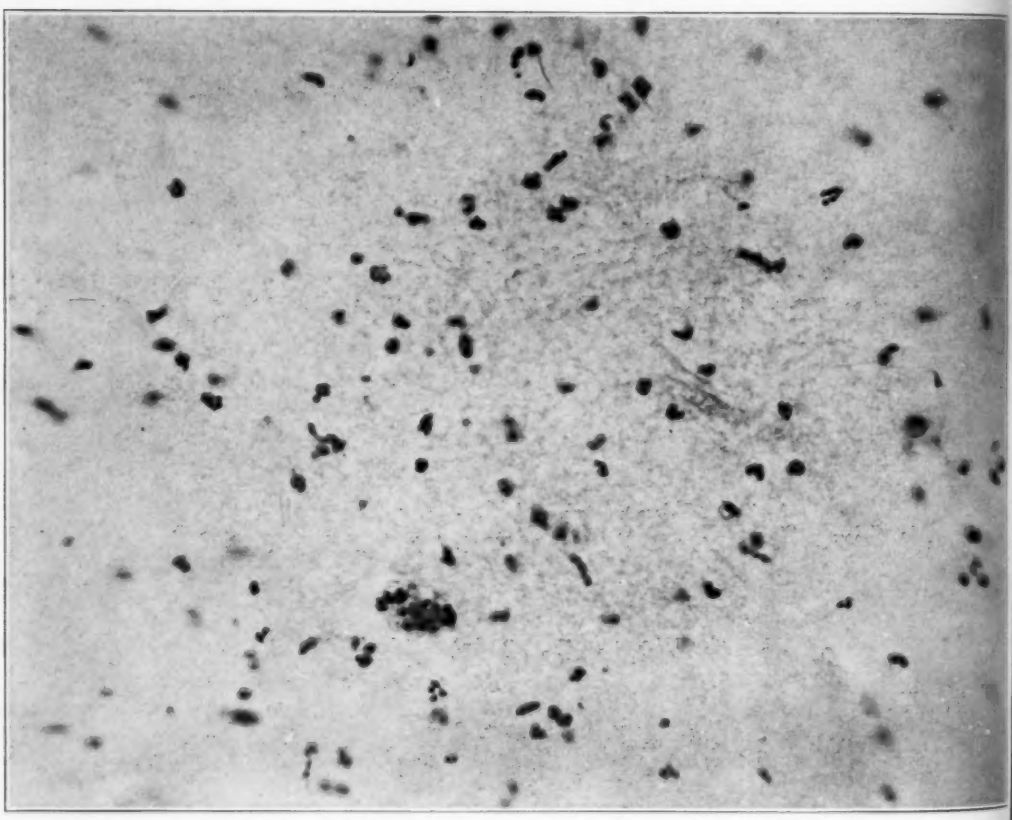

Fig. 2.—Polymorphonuclear neutrophilic leukocytes scattered through the brain at the eight and one-half hour stage.

the light they shed on the mechanism which permitted the infiltration of the brain with polymorphonuclear leukocytes and the origin of compound granular corpuscles, the observations are not relevant here.

The histopathologic picture is so constant that it can be described with brevity. In the infarcted areas of the brain in nineteen of the dogs, that is, in the animals killed from eight and one-half to ninety-six hours after the emboli were introduced, polymorphonuclear neutrophilic leukocytes were present. At the eight and one-half hour period they were present in the perivascular spaces in some numbers (fig. 1) in the leptomeninges over the area, and a few of these cells

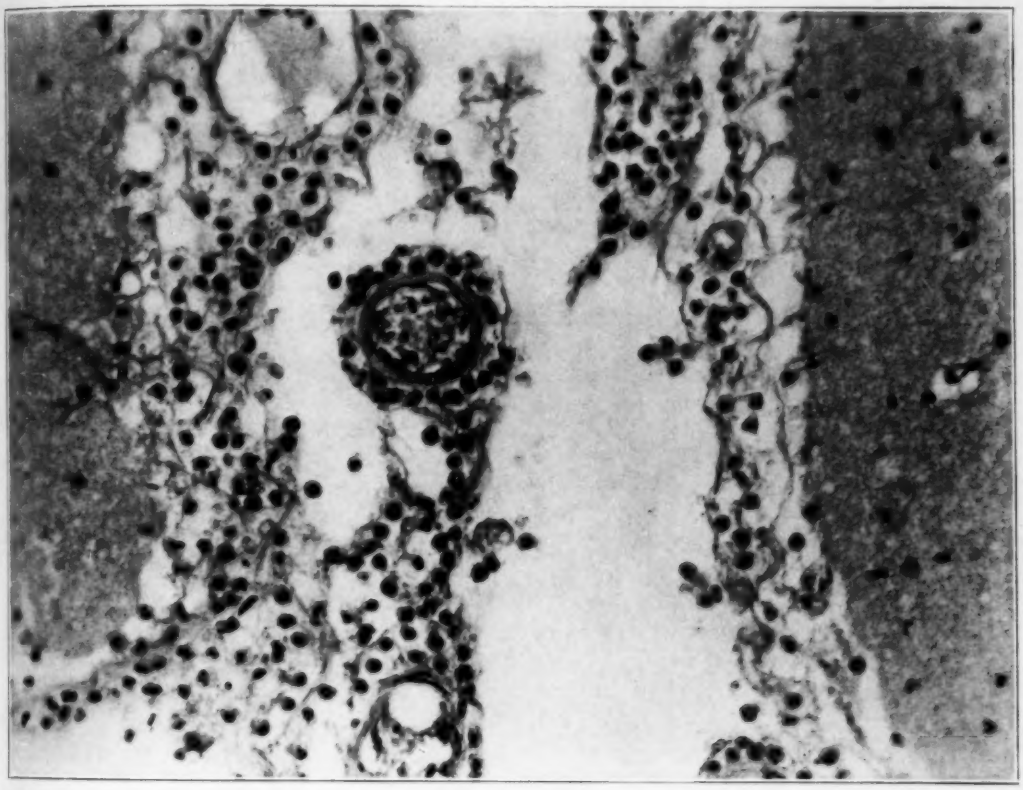

Fig. 3.—Reaction in the meninges suggesting meningitis of infectious origin (eighteen hours after embolism).

were scattered in the gray and white matter (fig. 2) away from vessels. At eighteen hours, the number present had strikingly increased (fig. 3). The increase continued through the twenty-four and thirty-eight hour stages and up to the forty-eight hour period when the greatest number were seen. At forty-eight and seventy-two hours, they packed the deeper layers of the cortex especially. Their location could be seen in the section with the unaided eye. It was indicated by a blue line about half the usual thickness of the gray matter. In all instances the leukocytic infiltration was heavier in the gray matter than in the white.

At the forty-eight hour and subsequent stages, the polymorphonuclear leukocytes began to degenerate. Their nuclei were pyknotic and many of their cell

boundaries had disappeared. Small clumps of chromatin material due to nuclear fragmentation were scattered about. After ninety-six hours had elapsed, the number of these cells was much reduced. At seven days, they were no longer present and compound granular corpuscles outlined the softened area (fig. 4).

The polymorphonuclear leukocytes invaded the infarcted area first by the perivascular spaces. Though they may have reached the subarachnoid space directly from the pial vessels, many seemed to have reached it by following the perivascular spaces of the cerebral vessels out to the point at which they joined with the subarachnoid space (figs. 5, 6 and 7). When the softened area bordered

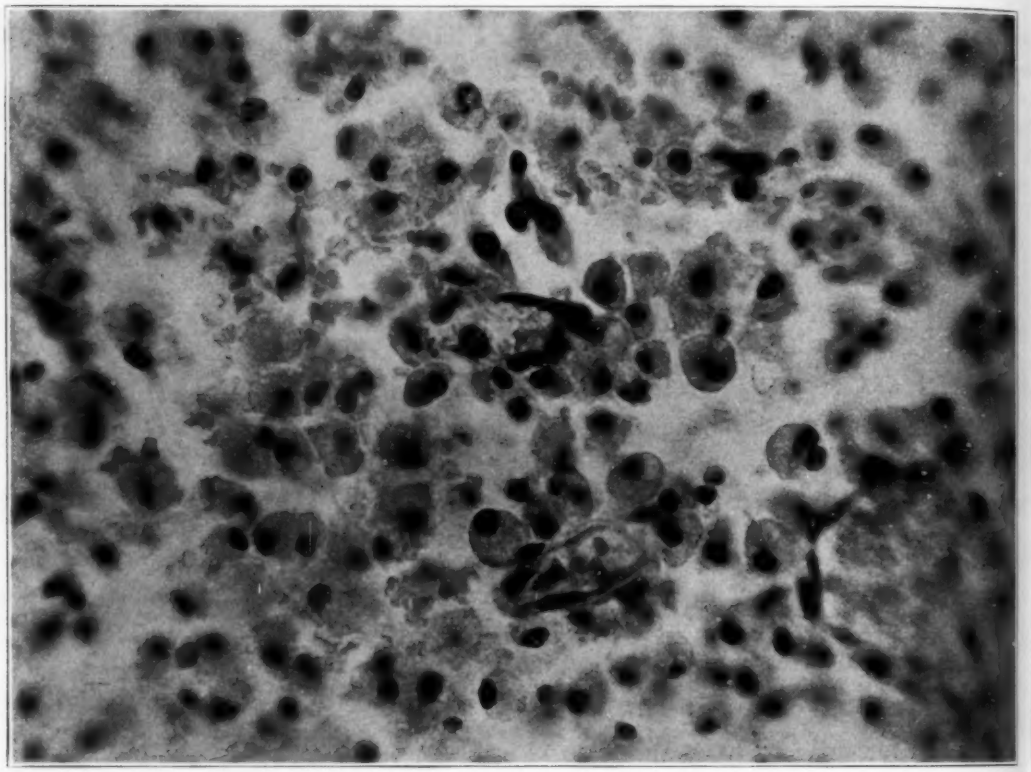

Fig. 4.—Typical compound granular corpuscles which have replaced the polymorphonuclear neutrophilic leukocytes (seven days after the infarction).

the ventricle, the ependyma was degenerated and cerebrospinal fluid came in direct contact with the degenerating area. In later periods the leukocytes respected no boundaries and were diffusely scattered in all parts of the softened area.

No organisms were present either with the eosin-methylene blue stains or with the Gram's stains in any of the twenty animals included.

It was in the explanation of the mechanism by which polymorphonuclear leukocytes were permitted to infiltrate widely the infarcted area that the special neuroglial stains were of value. Cajal's gold sublimate stain and Hortega's silver carbonate stain for astrocytes demonstrated the extreme destruction which

occurred in these cells. The perivascular feet of the astrocytes were fragmented, as were the rest of their projections and thus the normal barrier, usually so effective in preventing the passage of cells of hematogenous origin from the perivascular spaces into the parenchyma of the brain, was destroyed.

Red blood cells were present at times in the softened area and in the meninges over it. In the animals permitted to live seventy-two hours they were seen in the largest numbers. In some of the animals no hemorrhage had occurred.

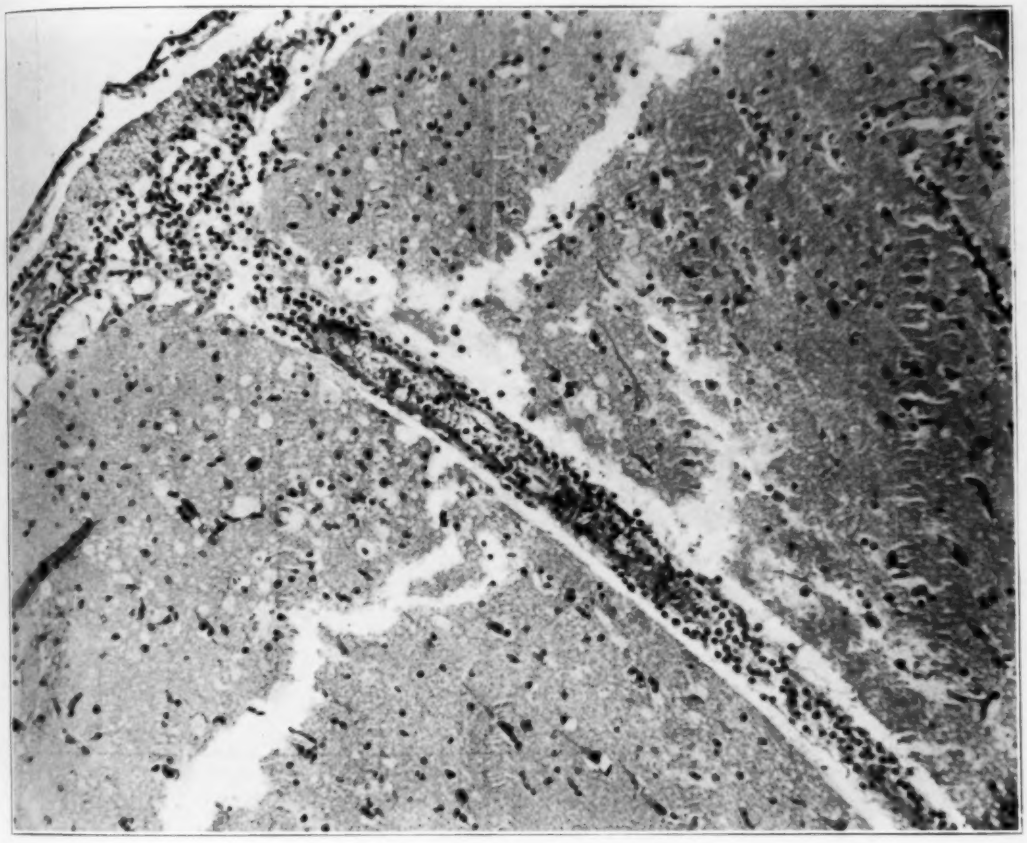

Fig. 5.—Polymorphonuclear neutrophilic leukocytes in the perivascular space of a cerebral vessel. They are extending from a deep area of cerebral softening to the subarachnoid space (eighteen hour stage).

It is of importance to note that the pathologic changes did not vary with the various materials used for the emboli. They varied only with the stage at which the specimens were studied.

The time of appearance of mononuclear phagocytes (compound granular corpuscles) is of interest here as it was these cells that replaced the polymorphonuclear leukocytes. They appeared in great numbers only after the polymorphonuclear cell reaction had reached its peak. A few wandering cells were

evident as early as the twenty-four hour period in both the brain and the leptomeninges. At the forty-eight hour stage, their number had increased. At seventy-two hours, they were more numerous, especially in the area near the vessels. At seven days, they were practically the only cells present in the softened area. In the leptomeninges their formation often took place by indirect cell division from cells of the perivascular tissue or from cells of the leptomeninges. In the brain, too, their origin could be traced from the perivascular sheaths and also from microglia cells at the periphery of the softened area. Specific staining methods demonstrated that neuroglia played no part in their formation.

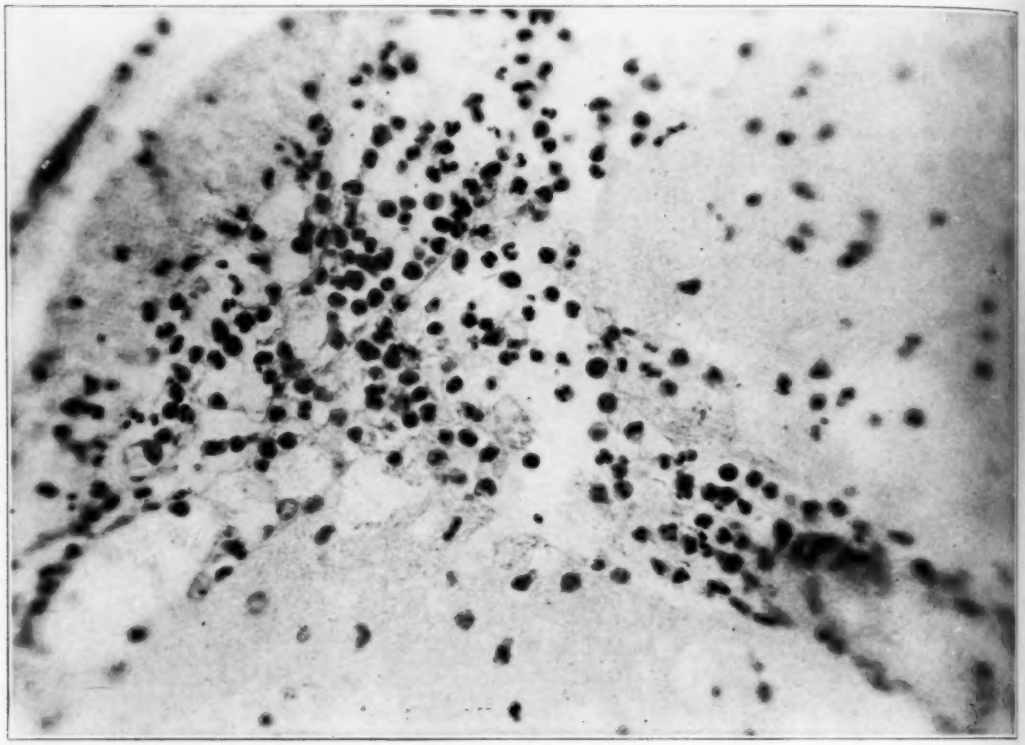

Fig. 6.—Polymorphonuclear leukocytes in the perivascular space of a cerebral vessel at its point of entrance through the leptomeninges (eighteen hour stage).

CEREBROSPINAL FLUID

An attempt was not made to obtain cerebrospinal fluid in two of the twenty experimental animals. In six animals fluid was not obtained by cisternal puncture. In several instances this was true even when the cisterna magna was exposed. It was interpreted as indicating an occluded cisterna magna, the result of the great increase of intracranial pressure caused by swelling of the affected hemisphere. Attempts at ventricular puncture made in a few of these six animals also failed

to yield fluid. In four dogs the cerebrospinal fluid was so bloody, as the result of trauma at puncture, that it was considered to be of no value for study. Thus twelve of the twenty experiments are incom-

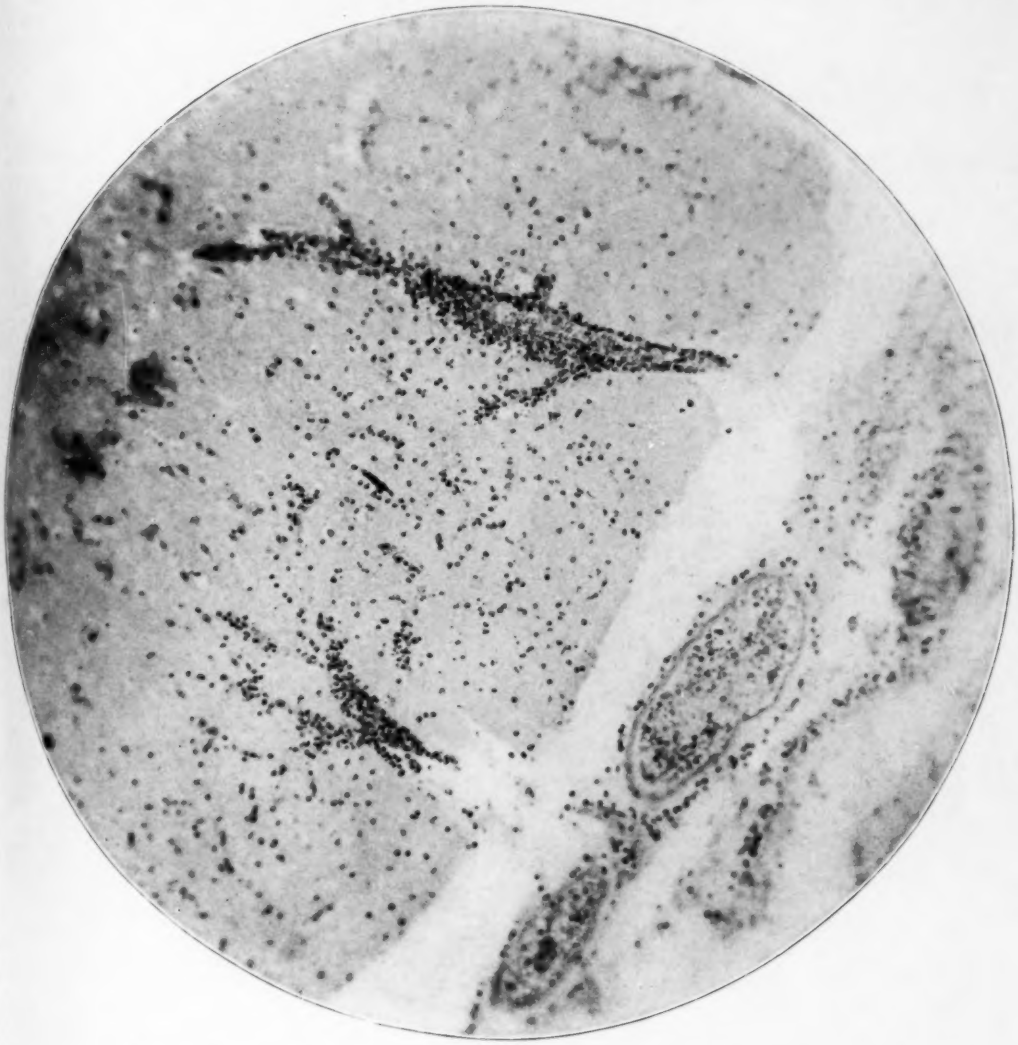

Fig. 7.—Perivascular accumulation of leukocytes in the perivascular spaces of cortical vessels. These cells are reaching the meninges by way of the perivascular spaces (twenty-four hour stage).

plete in that studies of the fluid are lacking. In the eight dogs left, however, specimens of cerebrospinal fluid satisfactory for study were obtained.

In the examination of the fluid the microscopic examination was made either at once or within a one hour period. Total counts were made in most instances. If red blood cells were present they were destroyed by acetic acid and a second total count made with a differential count. The remaining fluid was treated according to Alzheimer's method, that is, precipitation of the protein in the fluid

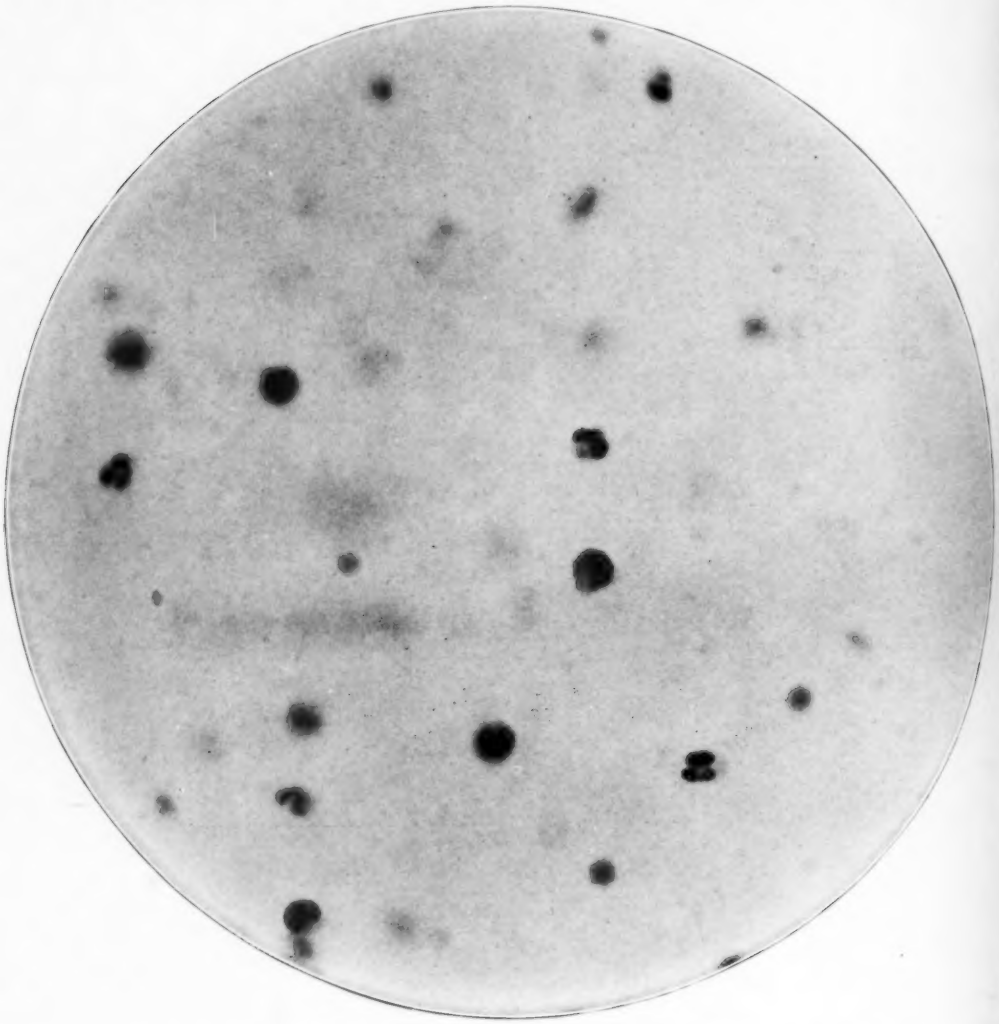

Fig. 8 (animal 16).—Preparation by Alzheimer's method of the cerebrospinal fluid of a dog (seventy-two hours after the embolism).

by the addition of a quantity of absolute alcohol equal to that of the fluid, centrifugating this mixture for two hours until the protein and cells were thrown down into a firm mass, and then embedding, cutting and staining this as for any histologic preparation. Alzheimer's method permitted accurate recognition of cell types.

In the cerebrospinal fluid treated in this way, polymorphonuclear leukocytes were demonstrated in six specimens, two taken at twenty-four hours after the ictus, one at thirty-eight, one at forty-eight and two at seventy-two hours (figs. 8 and 9). The greatest number found (1,135 per cubic millimeter) was in one animal permitted to live for seventy-two hours. The next greatest number, 371

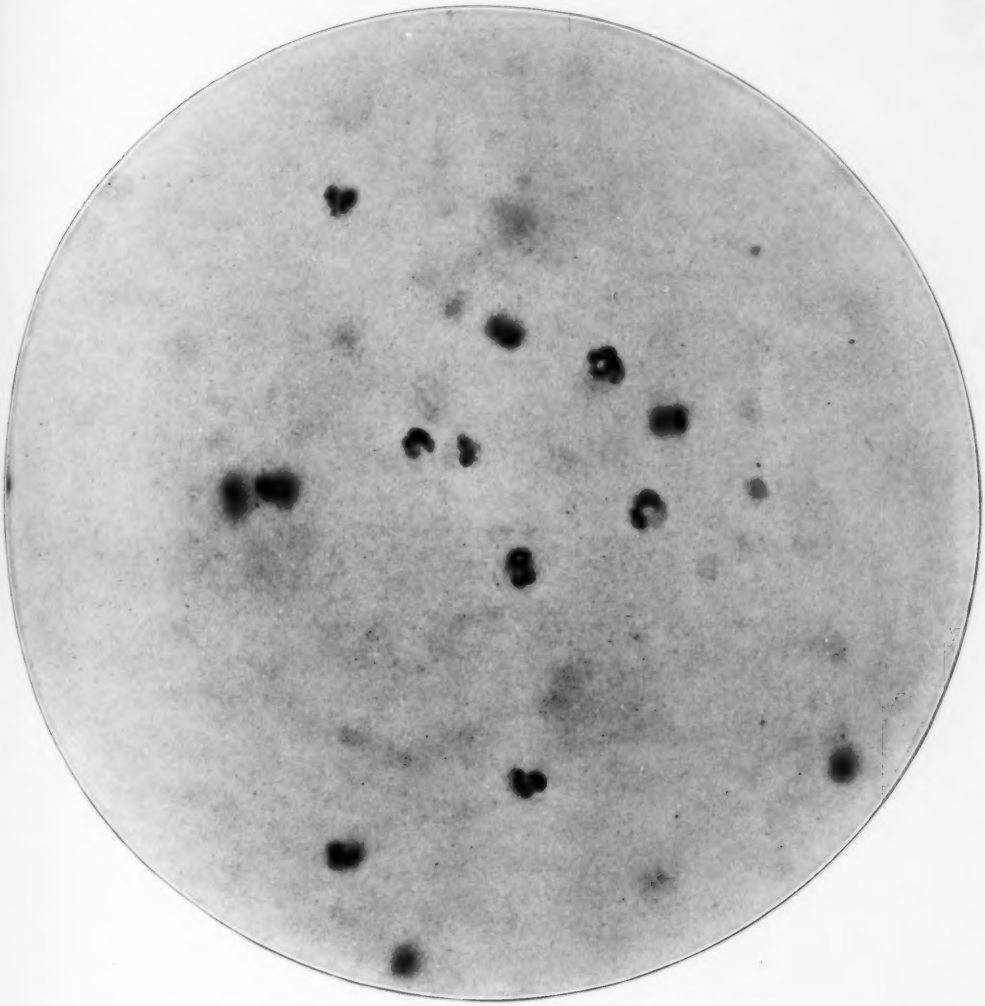

Fig. 9.—Polymorphonuclear leukocytes in the cerebrospinal fluid demonstrated by Alzheimer's method from animal 15 (seventy-two hours after embolism).

cells, occurred after twenty-four hours. It was our impression that the greatest number of cells occurred in the cerebrospinal fluid either when the area of softening bordered the ventricle destroying the ependyma, or when the infarction was superficial just beneath the pia. As long as the polymorphonuclear leukocytes persisted in these areas they might be found in the fluid. In two of the eight

Microscopic Observations

No.	Duration	Symptoms	Infarcted Area	Cerebrospinal Fluid
1	8½ hours	Severe convulsions	Polymorphonuclear leukocytes in leptomeninges and about vessels of brain	Traumatic blood at puncture; fluid not studied
2	18 hours	Hemiplegia	Polymorphonuclear leukocytes in brain and leptomeninges	Traumatic blood; not studied
3	About 24 hours (died)	Severe hemiplegia	As in no. 2	No fluid obtained
4	24 hours	Hemiparesis	Many polymorphonuclear leukocytes in brain and leptomeninges	Heavily blood-stained; unsatisfactory for differential count
5	24 hours	Slight hemiparesis	As in no. 4	Total cells 190 per cubic millimeter; after acetic acid 40 cells which were polymorphonuclear leukocytes; 6 polymorphonuclear leukocytes per high power field in centrifugated specimen with a few lymphocytes
6	24 hours	Hemiparesis	As in nos. 4 and 5	Fluid clear; no cells in counting chamber; a few cells in centrifugated specimen which were polymorphonuclear leukocytes and lymphocytes; considered negative
7	24 hours	Hemiparesis	As in nos. 4, 5 and 6	Total cell count 397 per cubic millimeter; after treating fluid with acetic acid 371 cells, 68 per cent of which seemed to be polymorphonuclear leukocytes in the counting chamber with 32 per cent mononuclears; in centrifugated specimen there were many polymorphonuclear leukocytes and a few mononuclears; fluid obtained by ventricular puncture
8	24 hours	Hemiparesis	As in nos. 4, 5, 6 and 7	No puncture done
9	38 hours	Hemiplegia	Many polymorphonuclear leukocytes scattered and in clumps in softened area and in leptomeninges	Total count 164 per cubic millimeter; no red blood cells; 151 polymorphonuclear leukocytes, 10 lymphocytes, 3 large mononuclear cells; in centrifugated specimen there were many polymorphonuclear leukocytes and a few lymphocytes; culture negative
10	44 hours	Hemiplegia	Many polymorphonuclear leukocytes with many of these cells showing degeneration in both brain and leptomeninges	No fluid obtained
11	44 hours	Hemiparesis	Many polymorphonuclear leukocytes in brain and leptomeninges, some showing degeneration	Red blood cells in fluid; when they were destroyed by acetic acid no cells were present
12	44 hours	Hemiparesis	As in no. 11	No fluid obtained
13*	44 hours	Hemiparesis	As in nos. 11 and 12; large pieces of brain from the infarcted area, including ventricle; softening was present up to the ventricle and the ependyma was destroyed; in the ventricle polymorphonuclear leukocytes were present; the tissue had been fixed in alcohol, embedded in cellodin and stained with toluidine blue	Traumatic blood at puncture; fluid not studied

Microscopic Observations—Continued

No.	Duration	Symptoms	Infarcted Area	Cerebrospinal Fluid
14	48 hours	Hemiplegia	Polymorphonuclear leukocytes and some wandering cells present in brain and leptomeninges; leukocytes showed much evidence of degeneration	Total cell count 94 per cubic millimeter; no red blood cells; in centrifugated specimen there were 6 polymorphonuclear leukocytes to the high power field; culture negative
15	72 hours	Hemiparesis	Polymorphonuclear leukocytes filling the area and present in leptomeninges; wandering cells in some numbers in brain and leptomeninges	Total cell count not made; in the centrifugated specimen there were many polymorphonuclear leukocytes and a few red blood cells; many of the leukocytes were degenerating
16	72 hours	Hemiplegia	As in no. 15 except that there were many areas of hemorrhage in the brain	Total cell count 4,500 per cubic millimeter; after acetic acid 1,135 polymorphonuclear leukocytes; in centrifugated specimen there were many polymorphonuclear cells, many of which were degenerating, some mononuclear wandering cells and some lymphocytes
17	72 hours	Hemiplegia	As in no. 15	No fluid obtained
18	72 hours	Hemiplegia	Polymorphonuclear leukocytes with many degenerating forms in brain and leptomeninges; mononuclear wandering cells also present; many hemorrhages in area	No fluid obtained
19	96 hours	Slight hemiparesis	A few polymorphonuclear leukocytes in small softened area in basal ganglia; some mononuclear wandering cells	No fluid obtained
20	7 days	Hemiplegia	Fat-filled wandering cells (compound granular corpuscles) filled the softened area; no polymorphonuclear leukocytes were present	No puncture done

* Had a satisfactory specimen of cerebrospinal fluid been obtained it would seem from the presence of polymorphonuclear cells within the ventricle in the sections that they would have been present in the fluid.

animals no white blood cells were found in the cerebrospinal fluid, though both animals showed a hemiparesis. One was allowed to live twenty-four hours and the other forty-four. In both of them, sections of the infarcted area showed polymorphonuclear leukocytes in the brain and in the leptomeninges. The infarcted areas were not large.

The accompanying table correlates the clinical data and the pathologic and cerebrospinal fluid observations.

REPORT OF CASES IN HUMAN BEINGS

Three cases of cerebral infarction due to noninfected emboli, all coming to necropsy within five and one-half days after the ictus, were available for study. Polymorphonuclear leukocytes filled the infarcted areas and were present in the leptomeninges in each instance. In the experimental material this period marked the upper limit of time at which polymorphonuclear leukocytes occurred. It would seem that in cases in human beings they persist for a longer period, for they showed little evidence of degeneration and few compound granular corpuscles were present.

Case 1.—G. S., a vocal teacher, aged 66, was treated in the Presbyterian Hospital in May, 1918, for cardiac decompensation, and the following diagnosis was made: chronic myocarditis, cardiac arrhythmia, premature contractions, general arteriosclerosis and hypertension. He was discharged as improved. He

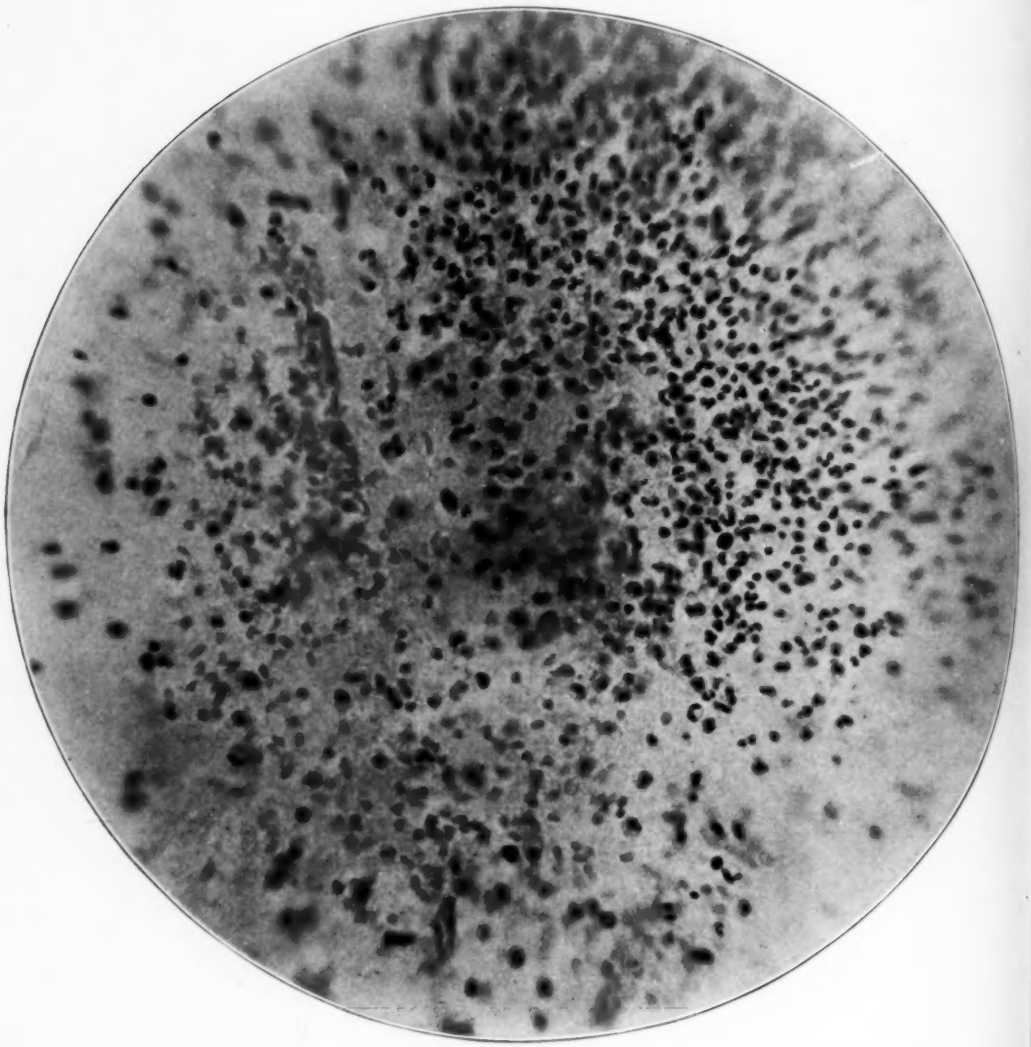

Fig. 10 (case 1).—Large focal collections of polymorphonuclear leukocytes in the brain, five days after the stroke. The reaction is so extreme as to suggest an intense infectious process.

was readmitted to the hospital on Dec. 1, 1920, in a semicomatose state. There was a right hemiplegia; the head was turned to the left, and he could not speak. He had been found in this condition on the morning of admission. The temperature

on admission was 100.4 F. On December 2, the white count was 12,500 and the blood pressure, 200 systolic and 105 diastolic. On December 4, the white count was 14,500. There was no growth in the blood culture made on December 4. On December 5, the patient's temperature reached 102.8 F. He died on this date, the fifth day of the illness.

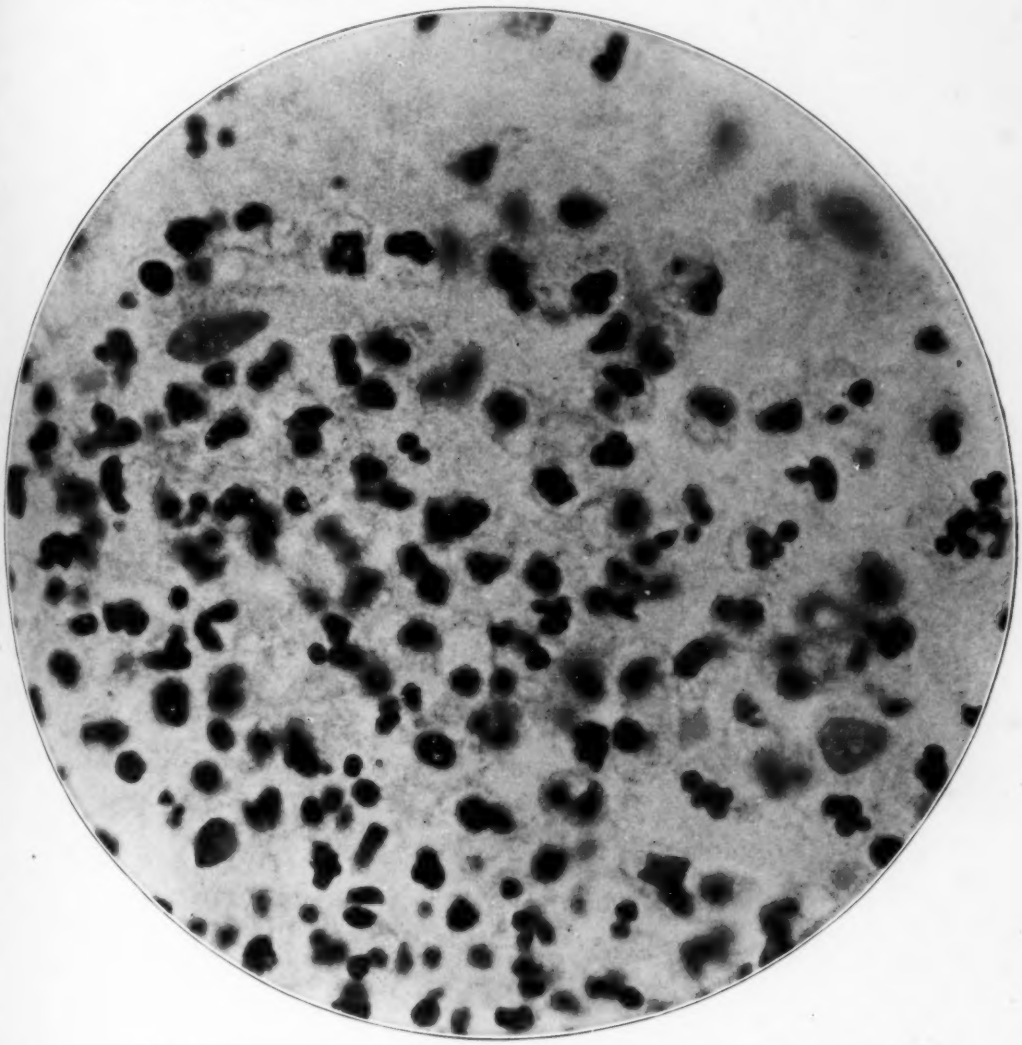

Fig. 11.—Photograph at higher magnification of the area seen in figure 10.

Necropsy.—The following diagnosis was made; thrombi of the left auricular appendage; embolus of the left middle cerebral artery; infarcts of the left cerebrum and right parietal lobe; generalized arteriosclerosis, especially of the coronary arteries, with calcification; cardiac hypertrophy; fibrous myocarditis; acute bronchitis; prostatic hypertrophy; acute prostatitis; hypertrophy and

dilatation of the urinary bladder with diverticula; healing infarct of the left kidney; bilateral hydrocele; fibrous pleural adhesions; emphysema.

Microscopically, the softened areas in the brain and overlying leptomeninges contained numbers of polymorphonuclear leukocytes and a few mononuclear phagocytes. There were also many small fresh hemorrhages. The polymorphonuclear leukocytes occurred especially in the deep layers of the cortex and were found here in dense (figs. 10 and 11) and in loose groups in the tissue, often without visible relationship to the vessels. The vessels extending from this area toward the pial surface contained polymorphonuclear leukocytes (fig. 12) in their perivascular spaces, and these cells were present in the subarachnoid space

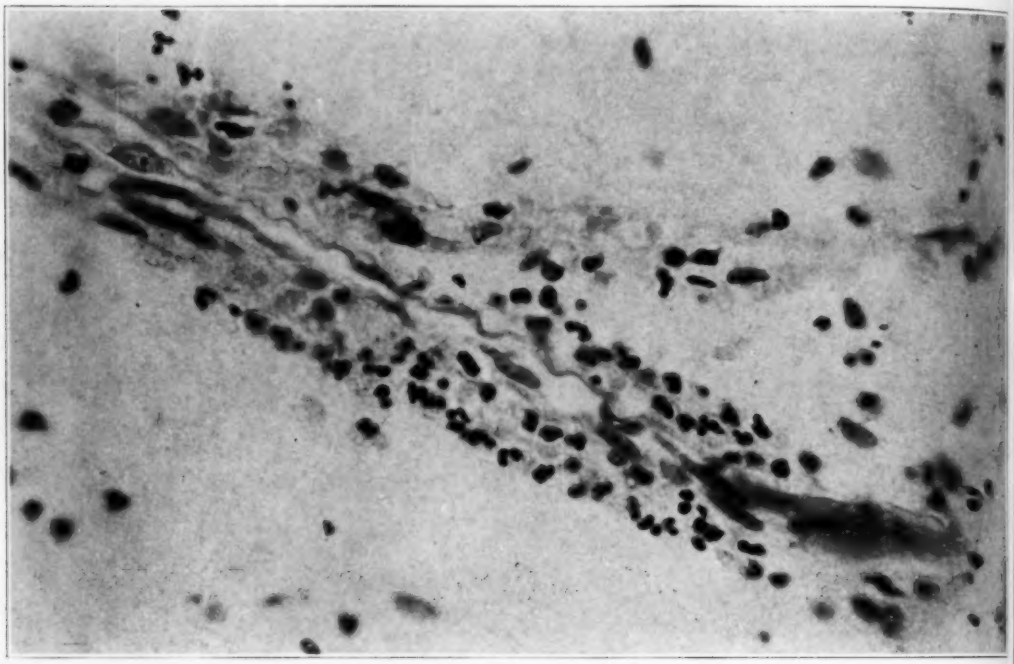

Fig. 12 (case 1).—Polymorphonuclear leukocytes in the perivascular space of a cortical vessel.

(fig. 13) in some numbers. Mononuclear phagocytes were present in relatively small numbers in the brain tissue and in the meninges.

No organisms could be stained among the accumulations of leukocytes in the infarcted area, in the emboli or in the thrombi from which the emboli arose.

Case 2.—J. C., aged 48, a housewife, entered the Presbyterian Hospital on Aug. 17, 1925, in a stuporous condition with a left hemiplegia. She had been treated in this hospital one and a half years previously, when a diagnosis of mitral disease and auricular fibrillation had been made. After this treatment she had remained well until the day before this admission, when she had suddenly become drowsy, then stuporous and finally paralyzed on the left side. During the forty-eight hours after entering the hospital, she regained some motion of the

left side and the stupor was less marked. On August 19, the white blood count, which had been 14,000 on admission, was 24,000, and 83 per cent of these were polymorphonuclear leukocytes. Blood cultures, taken on August 19 and 20, showed no growth. On August 20, the fourth day after the onset of the paralysis,

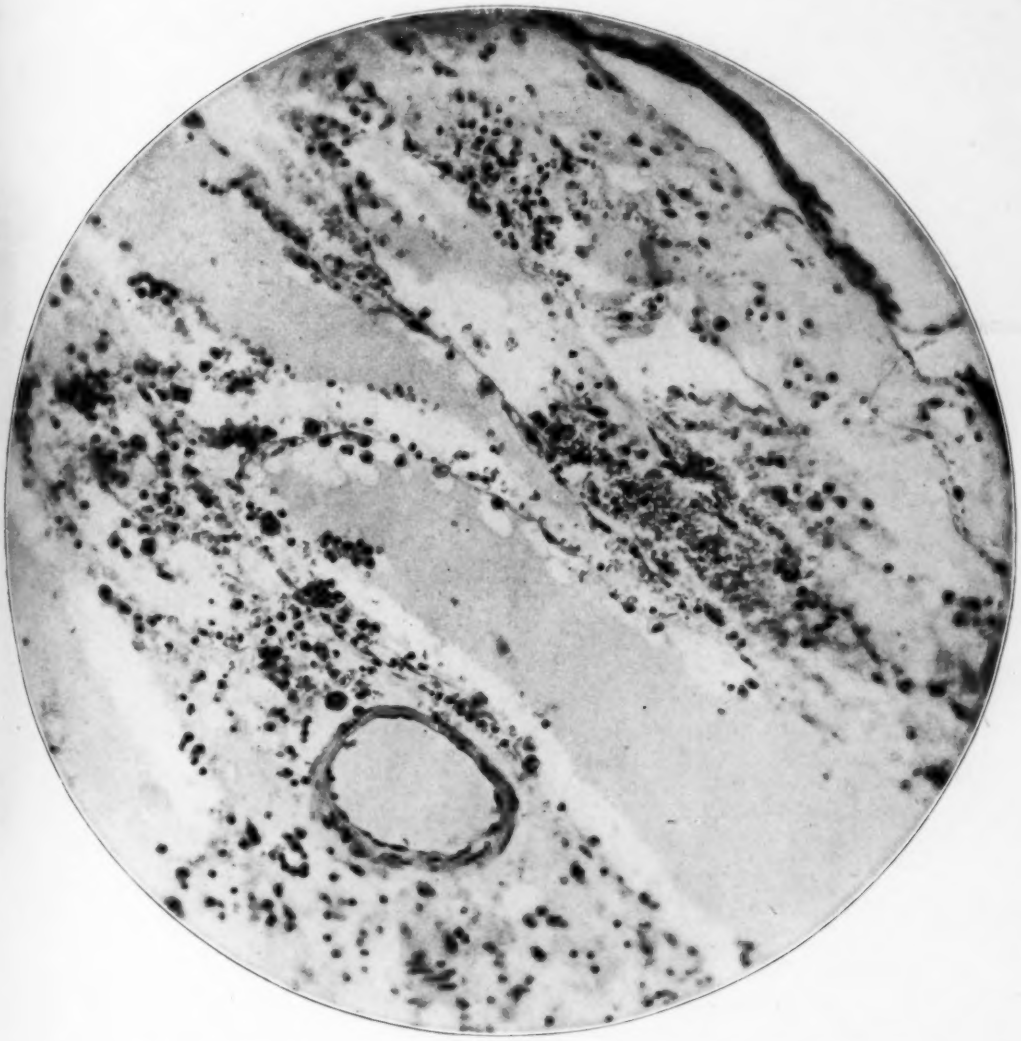

Fig. 13 (case 1).—Reaction in the meninges suggesting a mild infectious meningitis.

spinal puncture yielded clear fluid under slightly increased pressure. There were four lymphocytes per cubic millimeter. The test for globulin was negative. The patient's temperature rose slowly after the stroke until it reached 103.2 F. She died suddenly on August 21, the fifth day of the present illness.

Necropsy.—There were: thrombus of the left auricular appendage; embolus of the right middle cerebral artery; infarct of the right cerebrum; chronic cardiac valvular disease (mitral valve); mitral stenosis and insufficiency; cardiac hypertrophy and dilatation; infarct of the left lung; infarct of the left kidney;

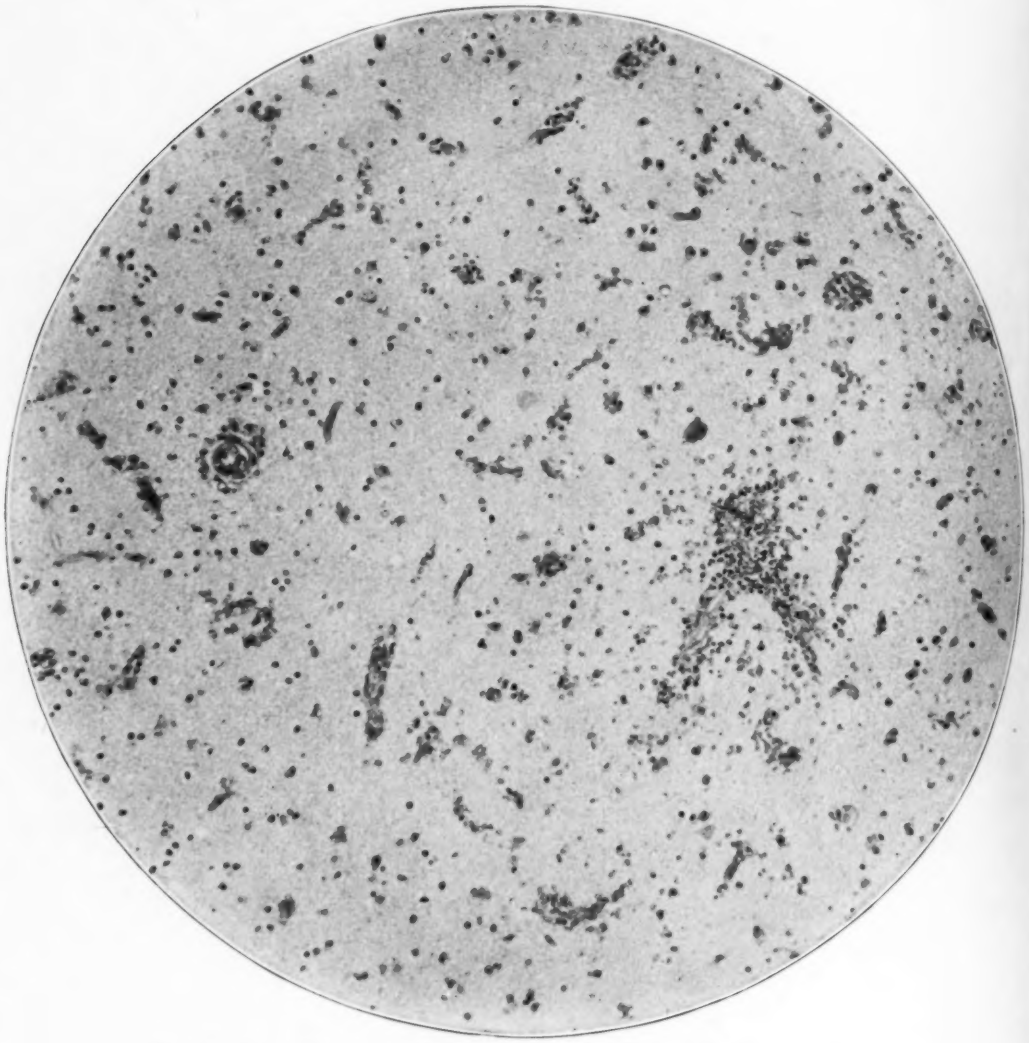

Fig. 14 (case 3).—Polymorphonuclear leukocytes in the perivascular spaces and scattered in the brain tissue, five days after the stroke.

chronic passive congestion of the liver and kidneys; subcutaneous edema; medial calcification of the aorta; hyalinization of the pulmonary venules; fibrous peritoneal adhesions.

The microscopic changes resembled in all respects those described in case 1 and in the experimental material. Again, at this stage, mononuclear phagocytes

were making their appearance. Stains for organisms in the sections of the brain also were negative.

CASE 3.—E. B., a carpenter, aged 68, had had signs of cardiac decompensation for five years before his final admission to the Presbyterian Hospital on Sept. 15, 1925. With treatment and rest at previous admissions he had regained compensation which was lost each time soon after discharge from the hospital. On the last admission he did not respond to therapy. He showed signs of pneumonia

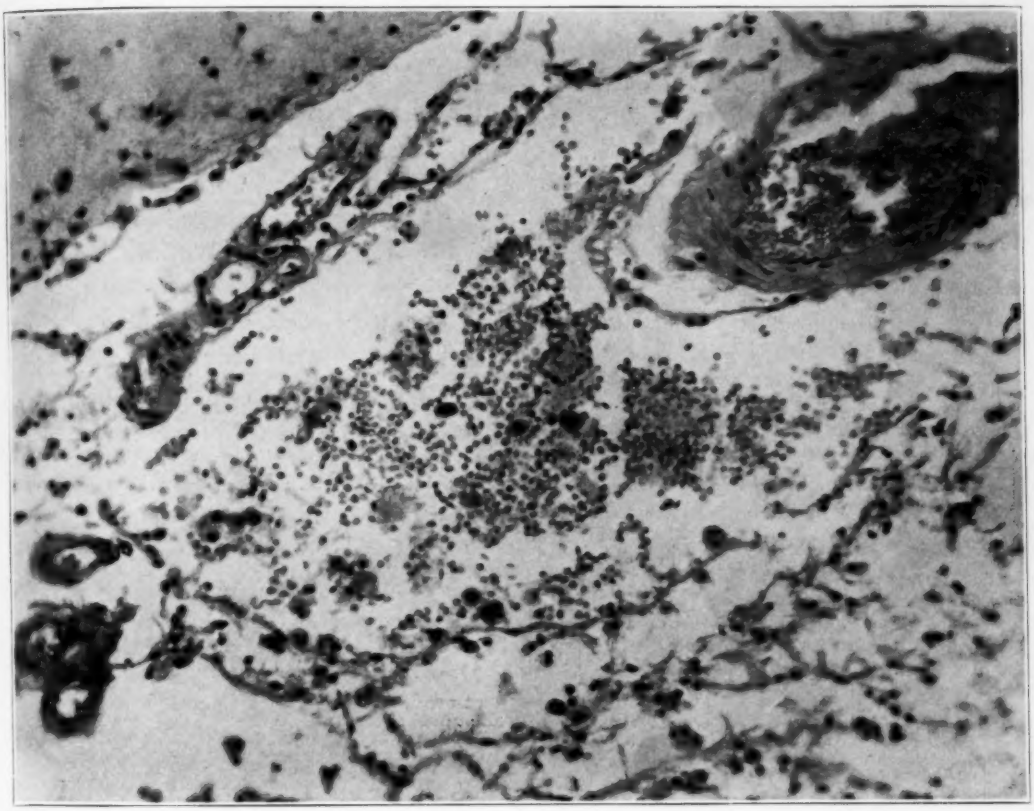

Fig. 15 (case 3).—Scattered polymorphonuclear leukocytes in the leptomeninges.

after October 9. Though previous blood cultures were negative, one taken on October 29 was reported to contain *Staphylococcus aureus* and a diphtheroid bacillus. This one positive blood culture was considered as due to a contamination. On October 31, he was found unconscious, and later examination revealed a paresis of the entire left side of the body. He died five and one-half days after the stroke.

Necropsy.—The anatomic diagnosis was: thrombi in the right auricle, right ventricle and left ventricle; embolus of the right middle cerebral artery; infarct of the right cerebrum; embolus of the left internal carotid artery;

rheumatic myocarditis, acute; cardiac hypertrophy and dilatation; rheumatic arteritis of the vessels in the testes and pancreas; chronic passive congestion of the lungs and liver; acute glomerulonephritis; acute prostatitis; lobular pneumonia, organizing; arteriosclerosis, mild; arteriosclerotic scars of the kidneys; adenoma of the kidney; cyst of the left epididymis; medial calcification of the aorta; fibrous pleural and peritoneal adhesions.

Microscopic study of the brain again revealed changes identical with those described in the other two cases. Polymorphonuclear leukocytes had infiltrated the infarcted area in large numbers (fig. 14), and were present in the leptomeninges (fig. 15). No organisms could be demonstrated in sections of the brain in the emboli or in the thrombi.

In two of the cases cited, the cerebrospinal fluid was not studied. In the one case, only sufficient spinal fluid was withdrawn to permit of a cell count and globulin test. We are forced, except in case 4 in which no autopsy was done, to borrow from the literature cases in human beings supporting our contention that polymorphonuclear leukocytes may be present in the cerebrospinal fluid in the early stages after cerebral embolism has occurred.

Case 4.—A. D., a salesman, aged 51, was admitted to the Royal Victoria Hospital on Feb. 21, 1930, with a history of acute dyspnea, a sensation of precordial tightness, sweats and abdominal and epigastric soreness of the left side. He had had periodic attacks of acute dyspnea associated with dizziness and dimness of vision for two years. Albumin had been found in the urine on several occasions.

On admission he was dyspneic and had a pulse deficit. The heart was enlarged to the left. There was marked congestion at the bases of the lungs and slight pitting edema of both ankles. Examination of the fundi revealed only slight evidence of arteriosclerosis. The blood pressure was 150 systolic and 100 diastolic. In the urine there was much albumin and blood. The white blood cell count was 8,400. The nonprotein nitrogen of the blood was slightly raised. Electrocardiograms gave evidence of myocardial damage compatible with coronary disease. The Wassermann reaction of the blood was negative.

The patient improved markedly under treatment. As he was being examined, previous to being discharged from the hospital, a complete paralysis of the left side of the body suddenly developed; breathing became stertorous, and he was confused. He became stuporous and died forty hours after the stroke. The white blood cell count thirty hours after the cerebral accident was 12,800, with 79 per cent polymorphonuclear cells in the differential count. The temperature rose from 98.3 at the onset to 102 F. at the thirty hour period, and went to 107 F. just before death.

Lumbar puncture done immediately after death gave clear fluid under increased pressure. The total cell count was 30 per cubic millimeter. Twenty-seven of these cells were polymorphonuclear leukocytes. The fluid was cultivated and there was no growth. The Wassermann reaction of the fluid was negative. Permission for a necropsy was refused.

The case was interpreted as one in which coronary disease was present and in which mural thrombi had formed. It was thought that from the thrombi an embolus had arisen which lodged in the right middle cerebral artery.

REVIEW OF THE LITERATURE

Polymorphonuclear Leukocytic Reaction in Acute Aseptic Destruction of Brain Tissue.—We are indebted first to Franz Nissl [1] for observations which are most helpful in aiding the interpretation of our observations. He pointed out that with acute destruction of nerve tissue multinucleated leukocytes pour into the damaged area. This reaction does not depend on how the damage was produced. It was the same after a wound made with a red-hot needle, a simple incision, the injection of a drop of blood or after the brain was frozen. He believed that the reaction was active and not passive. He emphasized that the polymorphonuclear leukocytes soon broke up in such lesions and shortly disappeared. He spoke of the reaction as being inflammatory.

Four years after Nissl's paper, Devaux [2] reported further observations on the reaction in brain tissue after injury with a red hot needle. He found that polymorphonuclear leukocytes appeared within twelve hours after the intervention, commenced to degenerate at twenty-four hours and had entirely disappeared at the end of the third day.

Farrar,[3] in the same year, reported on the mesodermal and ectodermal activities following the introduction of a foreign body into the brain. He inserted elder pith and found that polymorphonucleated leukocytes soon appeared in the area in which the brain had been damaged and rapidly filled the cavities in the pith. At six hours, polymorphonuclear leukocytic outpouring had started. It increased up to twenty-four hours when the maximum number were present. These cells then degenerated and disappeared rapidly. He regarded the outpouring as a passive reaction, the purpose of which was to fill space.

In the articles cited, the early reactions in destroyed brain tissue were studied after injury by outside noxious agents. Lhermitte and Schaeffer [4] desired to study the reactions following destruction from

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1. Nissl, Franz: Zur Histopathologie der paralytischen Rindenerkrankung, in Nissl and Alzheimer: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Berlin, Julius Springer, 1904, vol. 1, p. 315.

2. Devaux, Albert: Étude histologique des foyers de nécrose de l'écorce cérébrale, in Histologische und histopathologische Arbeiten über die Grosshirnrinde, 1904, vol. 2, p. 115.

3. Farrar, Clarence B.: On the Phenomena of Repair in the Cerebral Cortex: A Study of Mesodermal and Ectodermal Activities Following the Introduction of a Foreign Body, in Histologische und histopathologische Arbeiten über die Grosshirnrinde, 1908, vol. 2, p. 1.

4. Lhermitte and Schaeffer, H.: Les phénomènes réactionnels du ramollissement cérébral aseptique, leurs caractères differentiels avec l'encéphalite compliquée de ramollissement, Semaine méd. **30**:25, 1910.

within. They produced areas of softening by injecting sterile melted paraffin into the common carotid artery of dogs and one monkey. They studied the infarcted areas at varying periods of time after their production and described in detail the histopathologic changes resulting. The times at which polymorphonuclear leukocytes entered the infarcted area and disappeared from it agree essentially with our observations. They concluded from their work that the early reaction is inflammatory.

Correlation of Observations with Those Occurring in Other Body Tissues.—It is evident from a study of the literature of general pathology that this acute inflammatory reaction after aseptic destruction of body tissues is universal; it is well described in both old and recent works on the subject. Carscadden [5] (whose work is cited because the methods he used in the experimental production of tissue damage are similar to those used by Nissl on the brain) described the reaction in the liver, spleen, kidney, uterus and subcutaneous tissue of rabbits following aseptic incisions. In each tissue studied, polymorphonuclear leukocytes invaded the traumatized zone early, just as Nissl had shown they invaded the damaged brain. Karsner and Dwyer,[6] to cite again a piece of work in which the experimental methods used are comparable to those used by Lhermitte and Schaeffer and by us, described the reaction in the infarcted area in the heart after ligation of one of the branches of the coronary artery. Polymorphonuclear leukocytes appeared first about the larger capillaries, then infiltrated the interstitium. After forty-eight hours, there was a widespread invasion of the tissue in the infarcted area. The polymorphonuclear reaction in the heart in the early stage after aseptic coronary thrombosis in cases in human beings has often been described by pathologists.

The mechanism by which the polymorphonuclear leukocytes are called out is not clear. Carscadden suggested that histamine is liberated from the destroyed tissue, and that this causes vasodilatation and stasis, which permits the emigration of leukocytes. On the other hand, it is possible that tissue undergoing acute necrosis exerts a chemiotactic influence on leukocytes, which causes their emigration into the area. Karsner and Dwyer suggested this when they pointed out that the early removal of necrotic material is carried on by the polymorphonu-

5. Carscadden, W. G.: Early Inflammatory Reactions in Tissues Following Simple Injury, Arch. Path. **4**:329 (Sept.) 1927.

6. Karsner, H. T., and Dwyer, J. E.: Studies in Infarction: Experimental Bland Infarction of the Myocardium, Myocardial Regeneration and Cicatrization. J. M. Research **34**:21, 1916.

clear leukocyte. Our work suggests it also, for leukocytes in some instances had invaded destroyed nerve cells as they do in acute poliomyelitis.

Observations on the Cerebrospinal Fluid in Acute Cerebral Infarctions.—In the literature there is no large group of cases of infarction in man, the result of cerebral embolism or sudden thrombosis, in which the cerebrospinal fluid has been studied. However, single cases and small series of cases are reported in which polymorphonuclear leukocytes were found in the spinal fluid. In practically all of the instances, except in the case reported by Parker, final pathologic investigations correlating the reaction in the brain and that in the spinal fluid are either lacking entirely or the microscopic observations are not recorded in sufficient detail to be of value in this investigation.

In 1912, Babinski and Gendron [7] reported two cases of cerebral infarction in which the spinal fluid contained polymorphonuclear leukocytes. No evidence of infection was present in either case. In one there were 40 polymorphonuclear leukocytes per cubic millimeter and in the other 450. Claude and Oury [8] summarized the disease conditions of aseptic origin in which polymorphonuclear leukocytic reactions sometimes occur in the meninges and spinal fluid. They included in the group recent aseptic cerebral embolism and thrombosis. They quoted Lhermitte and Schaeffer's work and, carrying it a step further, stated that since polymorphonuclear leukocytes occur in the softened areas it is reasonable to suppose that they can reach the cerebrospinal fluid by the perivascular spaces, or that when the softened area is adjacent to the leptomeninges or ventricle they reach the fluid directly. Lhermitte and Schaeffer apparently did not study the spinal fluid during the stage at which the polymorphonuclear reaction was present in the brain, though they noted that they never found compound granular corpuscles in the fluid in the late stages.

Parker's case report [9] is the most valuable one we have found in the literature in support of our thesis. Apparently the middle cerebral artery was at first slowly compressed and then more rapidly and completely closed by compression by a tumor. On the first day after

7. Babinski, J., and Gendron, A.: Leucocytose du liquide céphalo-rachidien au cours du ramollissement de l'écorce cérébrale, Bull. et mém. Soc. méd. d. hôp. de Paris **33**:370, 1912.

8. Claude and Oury, P.: Réactions meningées et épanchements meningés puriformes aseptiques au cours des lésions en foyer de l'encéphale, Gaz. d. hôp. **96**:717, 1923.

9. Parker, H. L.: Tumor of the Brain Associated with Diffuse Softening and Turbid Cerebrospinal Fluid: Report of a Case, J. Neurol. & Psychopath. **10**:1, 1929.

hemiplegia developed, 1,600 polymorphonuclear leukocytes per cubic millimeter were found in the spinal fluid. There were no organisms in the smears and no growth in the cultures made. Autopsy, four days after the hemiplegia, showed a large area of infarction close to the ventricle. Polymorphonuclear leukocytes were present in the softened area in such numbers as to suggest an abscess.

COMMENT

When the reaction in the brain, the result of sudden infarction, first claimed our attention, we were confused and thought that we were dealing with an infectious process. One of the cases in our series was classified at first in the records as one of cerebral embolism of infectious origin, with secondary encephalitis and meningitis.

It is possible that at least some of the cases recorded in the literature as acute hemorrhagic encephalitis—fulminating cases in which polymorphonuclear leukocytes and red blood cells were found in the tissue at autopsy—may have been of embolic origin.

It is strange because of the intensity of the reaction, which is the constant result of sudden infarction, that the discovery of polymorphonuclear leukocytes in the cerebrospinal fluid is not of more frequent occurrence. At least one of the three possible pathways by which the cells can reach the fluid is always present. In the experimental animals and in the cases in human beings, polymorphonuclear leukocytes were always present in the leptomeninges. When the infarction involved the white matter or deeper layers of the cortex, they apparently had migrated along perivascular spaces to the meninges. When the softened area was superficial or when it involved the ventricular wall, the pathway was more direct.

From the clinical standpoint this report may aid in more accurate diagnosis. When a sudden or moderately sudden cerebral accident has occurred and polymorphonuclear leukocytes, but no organisms, are present in the cerebrospinal fluid, a cerebral infarction must be considered.

From the pathologic standpoint it may serve to point out again that in acute destruction of the brain from outside noxious agents or in that occurring from within, a reaction takes place which in its early phase is exudative or inflammatory. This reaction is frequently so intense as to suggest that an infectious agent is operative. This fact has been largely disregarded. If it is kept in mind one will not be tempted to regard the changes in simple trauma as essentially different from those in infectious processes, a difference that is not necessarily one of degree, but rather one of time. In the aseptic destruction the evidences of inflammation disappear early; in infectious processes they persist for a longer period.

CONCLUSIONS

1. Polymorphonuclear leukocytes pour out into an aseptically infarcted area of brain and into the overlying meninges eight and a half hours after the vessel to that part is blocked. They increase in number up to the forty-eight hour stage. The microscopic picture is one that suggests an infectious process. At seventy-two and ninety-six hours, these cells show progressive evidences of degeneration. At seven days they have been entirely replaced by compound granular corpuscles. The foregoing time relations are those that occur in the dog. In the cases in human beings available for study the reaction was the same, but the evolution of the process was somewhat less rapid.

2. During the phases at which polymorphonuclear leukocytes are found in the infarcted area, they may reach the cerebrospinal fluid in large or small numbers by way of the perivascular spaces of the vessels in the involved area, by direct invasion of the subarachnoid space from an adjacent area of softening or, when the infarcted area borders the ventricle, by extension directly into the ventricular fluid.

CEREBELLAR AGENESIS *

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The material on which this preliminary report is based consists of two adult brains which show marked deficiencies in the development of the cerebellum. For descriptive convenience, the brains will be designated and referred to as brain 1 and brain 2. Brain 1 was obtained from dissecting material in 1926, while brain 2 was found recently in an autopsy by Dr. Ernest Scott (Department of Pathology, Ohio State University), who kindly gave us the specimen. The ensuing report will deal briefly with: (1) the literature which has a direct bearing on cerebellar agenesis; (2) case histories, and (3) gross description. The microscopic description of these brains will form the subject matter of a later study.

LITERATURE

In this brief review of the literature on cerebellar agenesis, it should be borne in mind that reference will be made only to definite cases of agenesis. There are some cases which have been called agenesic, but which according to the descriptions given are cases of atrophy. The work published on cerebellar agenesis indicates the relatively independent development of the various parts of the cerebellum. Cases group themselves into deficiencies, complete or incomplete, of the right or left hemisphere, or vermis, or combinations of these.

Cases of complete agenesis are most interesting and extremely rare. The earliest recorded case of cerebellar agenesis is one of complete absence, and was described by Combette [1] in 1831. This was the brain of an epileptic idiot, 11 years of age, whose cerebellum was represented by a gelatinous membrane connected with the medulla by membranous peduncles.

Priestley [2] also described a case of complete absence.

A girl, aged 4 months, the second child of healthy parents and a full time baby, showed no vestige of the cerebellum, peduncles or pons. Priestley stated

* Submitted for publication, July 30, 1930.

* From the Department of Anatomy, Ohio State University.

1. Combette: Rev. méd., 1831.

2. Priestley, D.: Complete Absence of Cerebellum, Lancet **2**:1302 (Dec. 25) 1920.

that "on exposing the brain it was found to be extremely distended; the brain matter formed a thin layer over the ventricles, which contained about 1½ pints of clear fluid. The fourth ventricle was covered by a thin sheet (0.5 mm.) of tissue running from the corpora quadrigemina to the dorsal surface of the medulla. On the ventral surface, the pyramidal tracts appeared to run up to the corpora mammillaria. The base of the skull showed three pairs of fossae, but there was no tentorium cerebelli."

Unfortunately no microscopic descriptions are given of these two cases of complete agenesis.

Other cases approach complete absence. The work of Ferrier [3] deals with the brain of a feebleminded girl, aged 15, whose cerebellum was represented by a minute nodule, the pons and peduncles being absent.

The vermis may be involved separately, as is shown by the two cases of Solovtzoff [4] of complete absence of the vermis.

The right or the left hemisphere may be likewise defective or absent independently of the opposite side. Neuberger and Edinger [5] described the brain of a man, aged 46, in whom the greater part of the right half of the cerebellum was absent. The left hemisphere was normal in regard to shape, size and foliations, whereas the opposite hemisphere was apparently represented by a nodule the size of a hazelnut which projected from the vermis. All three cerebellar peduncles were present, though greatly reduced in size, on the right side, especially the brachium conjunctivum, which was formed by a narrow band of fibers. The olive of the right side was normal, while the opposite structure was almost absent, being represented by small areas of gray matter. The cerebellospinal tracts of both sides were present. The hindbrain nuclei, though present on both sides, were not symmetrically arranged. In regard to structure, microscopic examination showed that the left hemisphere and the representative portion of the right were structurally normal.

Strong [6] gave the clearest and most complete description, both gross and microscopic, of unilateral agenesis. This case was that of a girl, aged 3. Strong said:

The following structures were found to be markedly defective: The greater part of the left cerebellar hemisphere, possibly a part of the vermis and the left superior colliculus; the right inferior olivary nuclei, the right central tegmental

3. Ferrier, D.: Functions of the Brain, London, Smith, Elder & Co., 1886.

4. Solovtzoff, N.: Nouv. iconog. de la Salpétrière **14**:127, 1901.

5. Neuberger and Edinger: Einseitiger Fall totaler Mangel des Cerebellums, Berl. klin. Wchnschr., 1898, vol. 35, nos. 4 and 5.

6. Strong, O.: A Case of Unilateral Cerebellar Agenesia, J. Comp. Neurol. **25**:361, 1915.

tract and the left corpus restiforme; the left middle cerebellar peduncle, the right pons nuclei, the right pes and the right substantia nigra; the left nucleus dentatus, the left superior cerebellar peduncle and the right nucleus ruber.

The case reported by Salter [7] of complete absence of the left cerebellar hemisphere, vermis and left peduncles in an epileptic male appears to have had hydrocephalus as its causative factor, since the space usually occupied by the left cerebellar hemisphere was filled by the cerebrum.

The work of Langelaan [8] should be mentioned in view of the comparison with the stages of normal cerebellar development.

REPORT OF CASES

Clinical Histories.—Brain 1: The history of the white boy from whom brain 1 was obtained has been collected from four different sources: the foster father, a juvenile court worker, a guardian and a practical nurse at the State Farm for Feebleminded.

The boy was born of a mother who, one month after delivery, was committed to a hospital for the insane. Her mental condition was explained as being induced by her husband's accidental death one month before her confinement and by the resulting strained economic circumstances. At the age of 6 months, at which time the child was adopted, particular note was made of his weak back; otherwise, he appeared to be perfectly normal. He did not begin to walk until he was past 4 years of age. He slowly acquired the ability to walk about the house, but frequently fell. He spoke few words and would often shake his head as if in discomfort. As he grew older, he preferred not to move from his chair nor to take part in any activity. During this time, he was transferred from his foster parents to a paid guardian. His condition became gradually worse, and then he was sent to a state institution. His condition there during the seven years prior to death is expressed in the words of a practical nurse: "This boy had a low mentality, with habits characteristic of a low grade imbecile. He had to be fed. He could walk if helped, could bear his own weight, but was unwilling to stand, walked with legs partially doubled and never crawled. He never wanted to sit erect, usually slumping forward, and would straighten up only if food was held in front of him. He always slept in a doubled up position. He could hold his head erect and carried his arms partially flexed. He never spoke." He died at the age of 19 years of gastro-enteritis.

Brain 2: The history of the man from whom brain 2 was obtained is meager. Records show that he was 68 years old and that he was an inmate of a county home for several months prior to death. His mentality appeared normal, but he experienced considerable difficulty in walking and in equilibration. The cause of death was diagnosed as chronic endocarditis and encephalitis.

Anatomic Descriptions.—Brain 1: Pronounced abnormalities were evident in the medulla, and particularly was it obvious that the cerebellum was reduced to proportions approaching complete absence (figs. 1 and 2).

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7. Salter, H.: Tr. Path. Soc. London **4**:31, 1852-1853.

8. Langelaan, T.: Development of External Form of Human Cerebellum. Brain **42**:130 (June) 1919.

The stage of development of the cerebellum resembled most nearly that of a 13.6 mm. (His) and a 24 mm. embryo (Arey[9]), corresponding roughly to the development of the cerebellum in the middle of the third month (Langelaan[8]). The left side (fig. 3), which was further developed, presented a mass distribution similar to that in a 24 mm. embryo. Aside from the general division into lateral lobe and anlage of the vermis, cortical differentiation had taken place, as was evidenced by the folia on the surface which, curiously, ran in a longitudinal direction. This side covered most of the left inferior colliculus. The right side was more nearly like that of the 13.6 mm. embryo (His) and showed only a cortical differentiation in the region of the lateral lobe. Toward the midline, an undifferentiated rhomboid lip was evident. The cerebellar connections to the brain stem were also greatly diminished in size. The paths from the pons, which were not prominent, were small and could be seen behind the trigeminal nerve roots (fig. 2). The brachium conjunctivum was not externally defined.

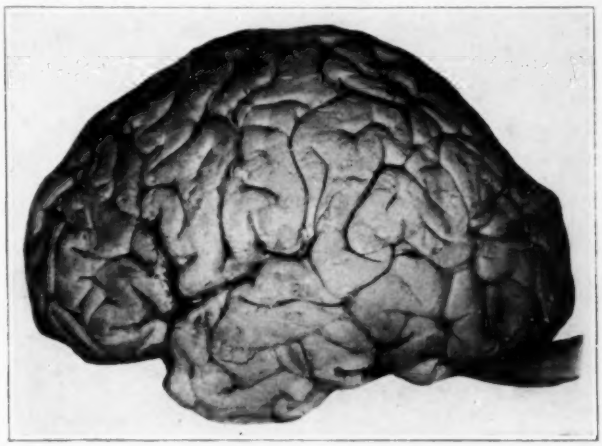

Fig. 1.—Lateral view of brain 1 from white male idiot, aged 19, showing absence of normal-sized cerebellum. The brain is shown reduced one-half.

The medulla presented externally two pronounced abnormalities, namely, the bilateral absence of the olives and the extreme width of the rhomboid fossa. The latter was flat, and by removing the ependyma it was seen that the three major characteristic divisions were absent. The inferior margins of the fossa were bounded by unusually prominent clavae, which faded out laterally. The lateral recesses had no inferior margins. The floor of the fossa did not present the usual prominent elevations, which may have been due to the flat condition of the fossa. The medial sulcus was ill defined and very shallow. The facial colliculus, superior fovea, locus coeruleus, trigonum hypoglossi, area acustica and stria medullaris could be defined, while the area of the ala cinerea and area postrema were poorly delimited. On the floor of the fourth ventricle, a double row of partially engorged blood vessels, which formed a series of dashlike marks about 1 mm. from the midline, pursued a longitudinal course. These vessels had a diameter of approximately 0.3 mm. The dimensions of the fossa were 30 by 25 mm., the greatest length and width, respectively.

9. Arey: Developmental Anatomy, Philadelphia, W. B. Saunders Company, 1926, p. 256.

The pons presented very little elevation on the anterior surface of the brain stem. No demarcation could be noted between the pons and the pyramids, and only a slight difference between the pons and the cerebral peduncles. The foramen cecum, however, was distinctly evident.

A dissection of the lateral ventricles was made primarily for an inspection of their condition and size, since in the majority of cases, as indicated in the literature reviewed, cerebellar atrophy is correlated with hydrocephalus. This inspection revealed the lateral ventricles to be normal and in every respect compatible with the descriptions of cerebellar deficiencies presumably caused by arrested development of certain portions of the cerebellum.

The arterial blood supply to the small amount of cerebellar tissue was meager and atypical. The left or larger half of the cerebellum had a blood supply slightly different from that of the right. From the adjacent posterior cerebral artery it received three branches which supplied the superior surface. Another vessel

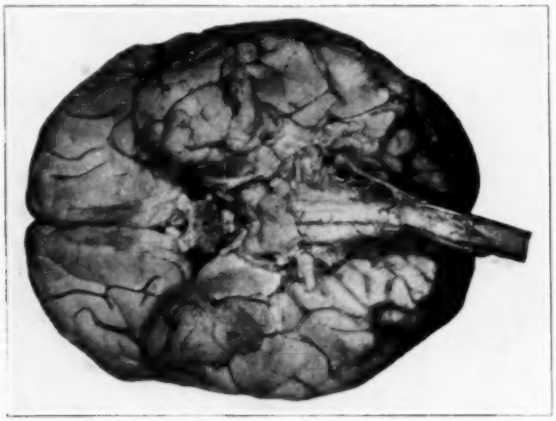

Fig. 2.—Inferior view of brain 1 (reduced one-half), showing almost complete absence of the cerebellum, poor demarcation of the pons from the medulla, asymmetry of the pons and indefinite pyramids. The blood vessels have been removed.

came to the superior surface as a branch from the basilar artery near the junction of the vertebrals. This branch no doubt corresponded to the anterior inferior cerebellar artery. All these branches were not over 0.3 mm. in diameter in the fixed state. The right side received three small vessels which were branches from the adjacent posterior cerebral artery, and which supplied the superior surface as did those on the left, and, in addition, it received from the posterior cerebral artery, just proximal to the posterior communicating artery, a small branch that passed inferiorly to the superior surface. This last branch was no doubt the representative of the superior cerebellar artery in embryonic life. These branches to the right side were likewise not over 0.3 mm. in diameter.

The venous blood outlet was through small branches on the superior surface, which joined the adjacent inferior cerebral veins and so drained into the superior petrosal sinuses.

Little diminution in the size of the main supply trunks to this region was noted, for the vertebrals were 3 mm. in diameter while the basilar was 4 mm.

A brief description of the posterior fossa and dura with some idea of the index of the skull may be of interest.

The posterior fossa had two well defined inferior occipital fossae of sufficient size to contain a normal cerebellum. The foramen magnum was in a plane inclined forward at an angle of about 60 degrees with the horizontal, in contrast to the normal almost horizontal plane.

The dura, as represented by the tentorium cerebelli, was well developed when the brain was removed, and separated the cerebral hemispheres above from the empty posterior fossa below.

The cephalic index of the skull, the bistephanic diameter and the glabellar-inion length being used, was 80.

Brain 2 (fig. 4): The scalp and calvarium were normal in thickness. The dura mater was slightly thickened, and the pia and the arachnoid, over the surface

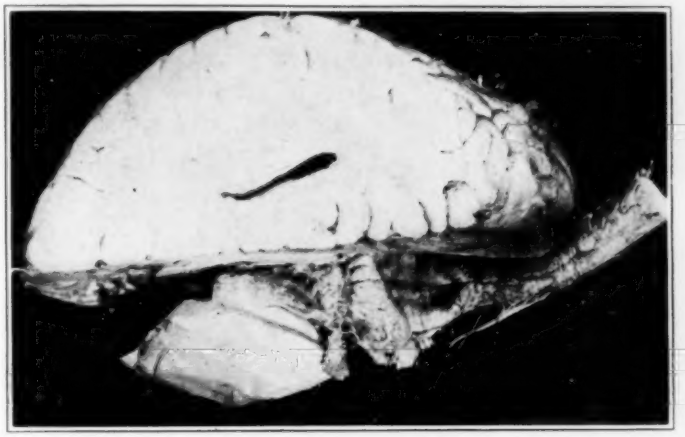

Fig. 3.—Superior view of brain 1 (reduced one-half) cut to show the rhombencephalon. The left side of the maldeveloped cerebellum and the flattened fourth ventricle are clearly shown. Note should be made of the normal lateral ventricle.

of the hemispheres, were congested and edematous. The meningeal vessels revealed a conspicuous and apparently sclerotic condition. At the base of the brain, the vessels were decidedly sclerotic. The meninges were not thickened. There was noted a marked deformity and malformation of the cerebellum in which the right lobe was normal in size and appearance; the left lobe was represented by a small irregularly shaped portion measuring approximately 2.5 by 1.5 cm. On examination of the base of the skull, it was found that the dural coverings of the cerebellum had adapted themselves to this malformation and showed only a space large enough for its accommodation. The bony development at the base of the skull was apparently normal. When the lateral ventricles were opened there was no evidence of hemorrhage or hydrocephalus. The choroid plexus of each side was somewhat swollen and edematous and contained rather numerous yellowish spots, varying from 2 to 4 mm. in diameter. The ventricular fluid was not increased. The medulla joined the pons at a slight angle (acute to the right) and appeared normal in all respects, except for the olive, which was absent on the right side. The clava of the left side was slightly larger than that

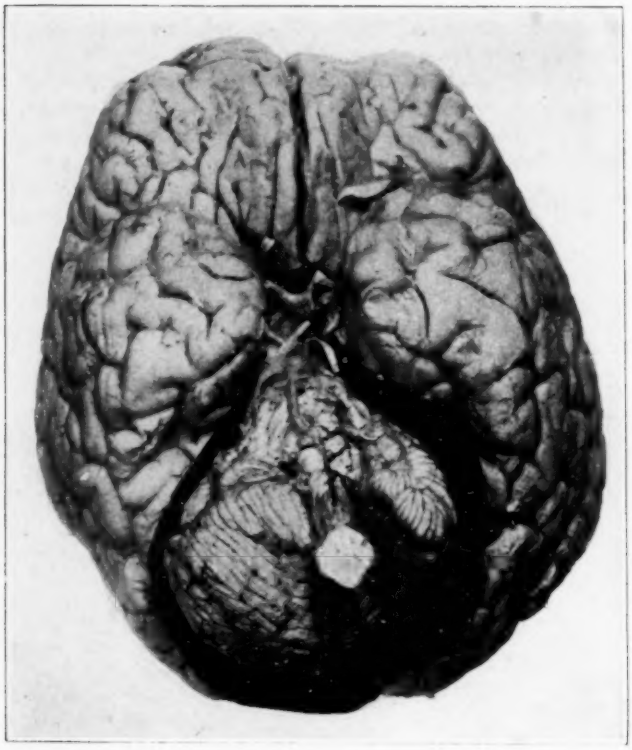

Fig. 4.—Inferior view of brain 2 from a white man, aged 68. A black background has been inserted behind the cerebellum to contrast the unequal size of the two cerebellar hemispheres. Comparison should be made of the divisions of the small left cerebellar hemisphere with figure 5. The specimen is shown reduced one-half.

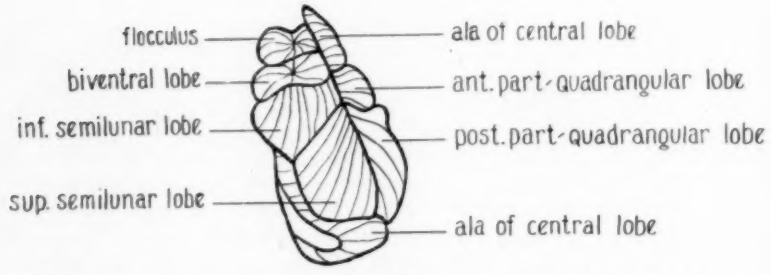

Fig. 5.—A diagram of the arrangement and names of the divisions of the maldeveloped left cerebellar hemisphere of brain 2 (B. N. A. terminology); actual size.

of the right side. Superficially, the fourth ventricle appeared in all respects to possess normal characteristics.

The pons was well developed and showed greater demarcation from the cerebral peduncle on the left side than on the right. The middle peduncle showed a greater development on the right side; that is, there were more contributing fibers, streaming free from the posterior end of the pons. The middle peduncle of the left side was smaller and was of greater size in the central and ventral part of the pons. Otherwise, the two sides were symmetrical.

The cerebellum presented a normal right hemisphere and a greatly diminished representative of the left hemisphere. The vermis was absent. The volume of the left hemisphere was approximately one eighth of that of the right. A more detailed examination showed this hemisphere to be unquestionably agenesic, for all divisions were clearly represented in diminutive form, each having the normal foliated arrangement of gray and white matter. From the folia, the white fibers could be traced by a separation of the adjacent divisions, while the larger group of fibers was contributed by the ala of the central lobe which presented the largest surface area. The diagram (fig. 5) indicates the divisions of the agenesic hemisphere shown in the photograph (fig. 4).

All cranial nerves and blood vessels on both sides of the brain were present, symmetrical and of normal size.

A CASE OF AGRAMMATISM IN THE ENGLISH LANGUAGE

A CLINICAL STUDY IN CATEGORIAL THOUGHT *

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In his study of agrammatism, Pick [1] lamented the fact that no investigation of the subject had yet been forthcoming in the English language. Such an investigation, he claimed, is "one of the desiderata for a future clarification of the aphasias." In the seventeen years that have elapsed since these words were written, no such study has issued from the pen of an English writer, while the German literature produced, in the same period, no less than four fundamental contributions to the subject (Salomon,[2] Isserlin,[3] Bonhoeffer [4] and Kleist [5]).

This failure on the part of English writers to investigate the agrammatical disturbances is all the more conspicuous, as the occurrence of agrammatisms has been consistently noted and mentioned by such workers as Broadbent,[6] Charlton Bastian,[7] Ross,[8] Mills [9] and Head.[10] The fact that agrammatism was noted and mentioned, but not studied, suggests the possibility that "typical" cases of agrammatism suitable for detailed study are either rare or rudimentary among English-speaking patients. If this possibility is granted, a thoroughgoing difference must

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1. Pick, A.: Die agrammatischen Sprachstoerungen, Berlin, Julius Springer, 1913.

2. Salomon, E.: Motorische Aphasie mit Agrammatismus, Monatschr. f. Psychiat. u. Neurol. **35**:181, 1914.

3. Isserlin, M.: Ueber Agrammatismus, Ztschr. f. d. ges. Neurol. u. Psychiat. **75**:332, 1922.

4. Bonhoeffer, K.: Zur Klinik und Lokalisation des Agrammatismus, Monatschr. f. Psychiat. u. Neurol. **54**:11, 1923.

5. Kleist, K.: Ueber Leitungsaphasie und grammatische Stoerungen, Monatschr. f. Psychiat. u. Neurol. **40**:118, 1916.

6. Broadbent, W. H.: On a Particular Form of Amnesia (Loss of Nouns), Med.-Chir. Soc. Tr., Lond. **49**:249, 1884.

7. Bastian, H. C.: Some Problems in Connection with Aphasia and Other Speech Defects, Lancet **1**:933 (April 3) 1897.

8. Ross, J.: On Aphasia, London, J. & A. Churchill, 1887.

9. Mills, C. K.: Treatment of Aphasia by Training, J. A. M. A. **43**:1940 (Dec. 24) 1904.

10. Head, H.: Speech and Cerebral Localization, Brain **46**:355 (Nov.) 1923.

be assumed between the structures of the English and German languages, respectively. Such a difference can, of course, not be posited between German and English patients.

Kussmaul [11] and Pick [1] pointed to the fact that, according to grammarians, languages in general fall into two groups with regard to their grammatical structure. At one end of the scale stands Eskimo with a bewildering abundance of grammatical formations, at the other end Chinese with a unique poverty of grammatical structures. They add that the German and Latin grammars approach, in point of complexity, the status of Eskimo, while English approximates Chinese in point of grammatical simplicity. Jespersen [12] took a similar view. If one is to trust the testimony of these authors, English represents a type of language that in the course of evolution has managed to simplify its structure, while German has retained the dead weight of a cumbersome grammatical organization which makes the language extremely complex and difficult to handle. On the basis of this consideration, the essential difference between the two languages is reduced to one of simplicity and complexity, and it would be understood that a patient afflicted with speech distress ("Sprachnot") will find greater difficulty in manipulating the involved German language than its simplified English counterpart. Agrammatism would, then, be dissolved into a difficulty, not of mastering grammar in particular, but of manipulating complex speech elements in general.

I was privileged, through the courtesy of Dr. Hassin, to study a case of aphasia, from his service at the Edward Hines Junior Memorial Hospital, with speech disturbances which, according to the German classification, constituted agrammatism.

REPORT OF CASE

History.—A white man, aged 38, in July, 1929, developed a high fever, followed after twenty-four hours by a paralysis of the entire right side with loss of speech. He recognized his environment and carried out simple orders. Sensibility was not disturbed. The ocular fundi were normal; no hemianopia seemed to be present. The pupils were equal and regular and reacted to light and in accommodation. The Wassermann reaction of the blood was negative. A spinal puncture was not made at that time. There was no history of syphilis, and the patient said that he had not had gonorrhea. The personal and family histories were irrelevant.

Examination.—On September 6, the patient was admitted to the Edward Hines Junior Memorial Hospital. The record says: "There is a complete right-sided hemiplegia. The right arm hangs limply by the side. Patient is unable to close his right hand or to spread the fingers. He makes no attempt whatever to use

11. Kussmaul, A.: Die Stoerungen der Sprache, Leipzig, F. C. W. Vogel, 1877.

12. Jespersen, O.: The Philosophy of Grammar, New York, Henry Holt & Company, 1924.

this hand in dressing or undressing himself. He has a spastic gait and drags the toes of the right foot. The muscle power is markedly diminished in the right arm, less so in the right leg. The tongue protrudes toward the right side and shows a slight tremor. All of the upper tendon reflexes are exaggerated on the right side. The right patellar reflex is also increased. There is a right ankle clonus and an inconstant right Babinski sign. Both abdominal reflexes are sluggish and both cremasteric reflexes absent."

Laboratory Examinations.—The urine was normal. The blood contained 15,200 white corpuscles per cubic millimeter, of which 58 per cent were polymorphonuclear leukocytes and 34 per cent lymphocytes. The Wassermann reaction was negative both with the blood and with the spinal fluid. The Lange gold reaction was 0122210000. The fluid was slightly bloody, but became clear after sedimentation. A cell count was not made.

The following entry, made by Dr. Anderson, was found with regard to the patient's mental behavior: "Patient is apparently fairly clear as to his surroundings; he is able to find his way about the ward and goes up to the dining room. He has a partial motor aphasia and expresses himself with difficulty. He can name objects and is able to carry out simple commands but is unable to carry out complicated orders or to name the use of objects. He has shown no abnormal behavior since his admission to the hospital."

Reexamination.—I saw the patient on November 16. The condition was the same with regard to the physical symptoms, except that some sensory changes were noted which were not in the record. The response to touch, pain and temperature was normal throughout. Localization was perhaps somewhat reduced on the right side but was generally well preserved. The patient was well able to indicate with his left hand where he was touched on the right side. Position and vibration sense were slightly diminished on the right side. However, any position given to the fingers or the hand of the right side was indicated correctly by the corresponding fingers and the hand of the left side. The response was merely delayed. There was total astereognosis of the right hand, both for objects (watch, pencil, tongue depressor, etc.) and for qualities (roughness or softness of paper, wood, metal, rubber, etc.). It was properly ascertained that the patient was able to name these objects and qualities when they were shown him at the time of testing for astereognosis.

On the day of reexamination, November 16, the patient had a fair ability to use spontaneous speech. He spoke in well formed sentences, though with some difficulty in finding words. No agrammatism was noted in spontaneous speech. He was well able to point to objects named verbally or in print, to name the objects indicated by the examiner and to designate the use of objects. Writing to dictation was practically impossible, both for letters, syllables and words. Copying was done well, both from print and from cursive handwriting. (The patient's left hand had been trained at the hospital.) Words were repeated correctly, regardless of the number of syllables and the nature of their contents (sense or nonsense). Reading aloud was fair for most words. When given a sentence or paragraph to read, however, he left out many words and combinations of words, giving the distinct impression of agrammatical reading.

The agrammatical disturbance being confined to reading aloud only, the case represented a rare instance of an agrammatical disturbance in an isolated faculty of speech and called for detailed study.

To study an aphasic person means to study his psychologic and linguistic responses to questions or orders. The obvious inference is that tests applied to aphasic persons are of limited value unless they conform to the standards of both psychologic and linguistic procedures. In other words, the tests must be psycholinguistic. In addition, tests of no matter what kind are useless for the purpose of retesting unless they are thoroughly standardized. To my knowledge, there are only two instances available in the literature of systematized tests for aphasic persons, the test series proposed by Head [13] and that by Salomon.[2] Head's series is thoroughly standardized, but is oriented neither on linguistic nor on psychologic principles. Salomon's series can hardly be termed standardized, and the grammatical and psychologic principles on which it is based are rather arbitrary and conform to no recognized norm. Since the available test methods were, thus, unsuited for the purpose in hand, a specially constructed method was evolved and applied to the various speech functions.

METHODS AND RESULTS

1. Each test consisted of sixty words and thus afforded an adequate basis for comparison.

2. Each test was repeated at least three times at intervals ranging from three days to one month.

3. The tests followed closely the traditional division of grammar into "parts of speech," "sentences" and "paragraphs."

4. The mistakes were classified as to their conformity or nonconformity to psychologic, logical and grammatical categories and tabulated as either "categorial" or "uncategorial."

5. In each test the time required for the performance was adequately measured in thirty second intervals, and thus a further basis for comparison was secured.

6. The identical series of tests was applied, with the necessary modifications, to the functions of reading aloud, mental reading, repeating, writing after exposure, writing to dictation and praxia. For the functions of spatial and temporal perception, of figuring, of apperception, memory and interpretation of pictures, special tests were used.

7. For each of these functions the minimal efficiency was ascertained and thus the residual efficiency ("span") charted.

8. Control tests on normal persons and on patients with lesions of the brain without speech disturbances were currently resorted to. They established the essential difference in the performances as to time and number of mistakes in this patient on the one hand, and in the subjects on the other hand.

9. The scoring was based primarily on the number of "uncategorial" mistakes. However, no rigid system of scoring was elaborated. It was merely assumed arbitrarily—for the purpose of this paper only—that a score of from one to five

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13. Head, H.: Aphasia and Kindred Disorders of Speech, Brain **43**:87 (July) 1920; footnote 10.

"uncategorial" mistakes was to be classed as "fair," that six or more "uncategorial" mistakes constituted a "poor" result, and that ten or more such mistakes were to be rated as a "failure."

10. All the tests consisting of isolated words were given both in large newspaper print and in typewritten samples. In addition, the words were placed both far apart and close together in order to ascertain whether variation in visual arrangement would yield a difference in results. No such difference was noted.

11. Writers on aphasia are wont to emphasize the importance of the fatigue factor in testing patients. I was unable to verify this statement in my patient. Even when tested for an hour and a half continuously, no perceptible signs of fatigue were noted. However, the possible influence of the factor was duly considered. To this end, each test, when given for the first time, was placed at the beginning of the testing hour. On a subsequent testing day it was placed in the middle of the hour, and, finally, at the end of the hour. The tests taken at the end of an hour showed, on an average, no notable variation from the other tests.

PRELIMINARY TESTS

These tests were given for the purpose of a cursory orientation without reference to psychologic or linguistic standardization. It developed that the patient was practically unable to read paragraphs. Thereupon he was given sentences, consisting of from three to seven words. Some of the sentences were read quickly and correctly, and some with great effort and considerable hesitation. In others the patient broke down completely. It was noted that the complete failures invariably resulted from phrases which contained particles, like "and," "in," "from," "you," etc.

He was then subjected to preliminary tests consisting of isolated words. The word series contained a miscellaneous assortment of nouns, adjectives, verbs and particles. Particles proved again the chief stumbling block for correct performance. Numerals, lettered figures and abbreviations like Mr., Mrs., Dr., etc., followed as close seconds. Nouns, adjectives and verbs seemed to enjoy a comparative immunity from linguistic mutilation.

After this preliminary orientation, systematic tests were resorted to in the following order:

READING ALOUD: A. PARTS OF SPEECH

1. *Nouns.*—(*a*) Monosyllabic Concrete Nouns: The patient was given sixty words like "lawn," "foe," "horse," "word," etc. The examiner had a typewritten copy with the individual words far enough apart to permit adequate registration of the mistakes. The mistakes were classed either as omissions, substitutions or additions of words, syllables and letters. Such terms as "grammatical," "syntactical," "paraphasic" or "contaminatory" were rejected as preempting. Thus, when the patient read "skirt" for "shirt," the mistake was marked as a substitution, not as a paraphasia.

Substitutions were grouped under two headings: categorial and uncategorial. When the patient substituted "father" for "dad," it was obvious that he had understood the meaning of the word "dad" and that he had substituted a synonym or a word belonging in the same category. Hence, the designation "categorial" mistake. Other "categorial" mistakes were, e.g., "girl" for "child," "wicked" for "vice." But "word" for "lot" indicated a complete missing of the appropriate category and was rated as an "uncategorial" mistake.

When "skirt" was read instead of "shirt," the mistake was one of literal substitution (k for h). But this involved an obliteration of the categorial meaning of the offered word and was classed as an "uncategorial" mistake.

"Grave" for "graves" constituted a literal omission; "cards" for "card" a literal addition. But in these malperformances, the categorial meaning of the words was preserved, hence their classification as "categorial" mistakes. In the latter instances the mistakes seemed to refer to a mismanagement of singular and plural. However, the term "grammatical" mistake was rejected. Whether or not any mistake was of a grammatical nature was to be proved by adequate tests, not decreed by the examiner's questionable conception of what constituted grammar.

Mistakes like "wife" for "life," "space" for "pace" referred to a substitution of words which both look and sound alike. From such errors it is impossible to infer whether the patient read primarily with the aid of visual or of auditory images. But if he misread "words" for "sword," it was obvious that what he substituted was two words that merely looked alike. This mistake was obviously made because of a misapprehension of the visual images. A mistake which would have pointed definitely to a misapprehension of the auditory image, like "tree" for "key," was never made, although the tests provided ample opportunity for such errors.

A type of mistake which threw valuable light on the mechanism of reading was classified as "transposition." It happened repeatedly that the patient transposed or changed the word sequence so that of two successive words the last was read first and the first last. For instance, instead of "bonds graves" he read "graves bonds" or instead of "desk road" he read "road desk." Since Erdmann and Dodge,[14] it is generally held by students of reading that the reader always tends to take in a plurality of words at one glance instead of reading word by word. In other words, the reader rushes ahead and anticipates words in advance of their actual pronunciation. But while the normal reader merely keeps these anticipated words "in mind" for future pronunciation, my patient proceeded immediately to pronounce the anticipated words. Later he corrected the mistake by adding the omitted word.

The test for monosyllabic concrete nouns was first applied on December 5. It was the first test of that day, followed by a series of other tests. The duration was two minutes and thirty-two seconds. Four categorial and four uncategorial mistakes were recorded. It was again applied on December 8, as the fourth test of the day. The result was nine categorial and two uncategorial mistakes in two minutes and forty seconds. A third application followed on Jan. 2, 1930, as the tenth test of the day. The result was seven categorial and two uncategorial mistakes in two minutes and two seconds. The total number of mistakes, therefore, was eight, eleven and nine, respectively, with a total median of nine. The number of uncategorial mistakes was four, two and two, with an uncategorial median of two. Since the number of uncategorial mistakes was kept below five, the result was rated as "fair."

(*b*) Monosyllabic Abstract Nouns: The patient was given sixty words like "day," "west," "death," "week," "feat," "game." The total median was six, the uncategorial median, four.

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14. Erdmann, B., and Dodge, R.: Psychologische Untersuchungen über das Lesen, Halle, M. Niemeyer, 1898.

(*c*) Bisyllabic Concrete Nouns:[15] Sixty words like "mother," "felon," "county," "robber," "army," etc., were given. The total median was six; the categorial median, none.[15]

(*d*) Bisyllabic Abstract Nouns:[15] Sixty words like "meeting," "business," "tariff," "mission," "effort," etc., were given. The total median was thirteen; the uncategorial median, none.[15]

(*e*) Polysyllabic Nouns: Sixty words like "example," "Washington," "candidates," "venison," etc., were given. The total median was twelve; the uncategorial median, four.

(*f*) Proper Names: Sixty words like "Lincoln," "Schmidt," "Meyer," "Canada," "Thursday," etc., were given. The total median was four; the uncategorial median, two.

(*g*) Compound Nouns: Sixty words like "armchair," "iron worker," "farmhand," "kingdom," etc., were given. The total median was nine; the uncategorial median, two.

Comment.—In none of the tests for nouns did the total for uncategorial mistakes exceed five. The conclusion was that the patient's control of nouns in general was "fair." In the series of polysyllabic nouns many words were included which consisted of a root and one or two affixes, e. g., "de-range-ment," "re-instate-ment." The patient showed a conspicuous tendency to leave out the affixes, like "re-," "de-," "-ment." This tendency to omit affixes seemed to be on a level with his tendency to leave out the plural affix "s" from the word "grave-s." This observation gave point to the assumption that the mismanagement of plural and singular was due less to a defect in grammar than to an urge toward simplification (Bréal,[16] Thumb and Marbe[17]), frequently mentioned in the linguistic literature.

The series of compound nouns yielded a striking minimum of uncategorial mistakes. On *a priori* grounds, it was to be expected that such compound nouns as "armchair," "doghouse" and "songbird" would offer greater difficulty to a man in speech distress than their isolated components, like "arm," "chair," "dog," etc. However, the experiment proved that the *a priori* conclusion, no matter how plausible, was wrong.

2. *Adjectives.*—(*a*) Monosyllabic Adjectives: The patient was given sixty words like "great," "dry," "slow," "cold," etc. The total median was two; the uncategorial median, two.

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15. The tests for bisyllabic words were by some unexplainable oversight not applied until February 20. In the meantime, the patient had progressed in handling nouns to the extent that he was well able to read nouns, except that he made mistakes in the endings. Uncategorial mistakes were no longer common. The tests cannot be used for comparison.

16. Bréal, M.: Semantics (English Translation), London, William Heinemann, 1900.

17. Thumb, A., and Marbe, K.: Die psychologischen Grundlagen der sprachlichen Analogiebildung, Leipzig, William Englemann, 1901.

(*b*) Bisyllabic Adjectives: Sixty words like "aimless," "careful," "public," "needy," etc., were given. The total median was seven; the uncategorial median, three.

(*c*) Polysyllabic Adjectives: Sixty words like "victorious," "prosperous," "romantic," etc., were given. The total median was seventeen; the uncategorial median, eight.

Comment.—In the monosyllabic and bisyllabic series of adjectives, the uncategorial medians were two and three. The performance was therefore rated as "fair." In the polysyllabic series, however, with an uncategorial median of eight, the patient had definitely exceeded his "span" of efficiency. The result was "poor."

3. *Adjectives Plus Nouns.*—Sixty word combinations like "happy parents," "undeserved praise," "difficult times," "expensive clothes," etc., were given. The total median was ten; the uncategorial median, two.

Comment.—This test is analogous to the test with compound nouns. It aims at combining in one single test the preceding word categories. The test contains a generous number of polysyllabic adjectives, like "undeserved," "difficult" and "expensive." These polysyllabic adjectives had given the patient particular difficulty. The *a priori* expectation was that, added to the nouns, they should only increase the difficulty of performance. But the experiment again refuted the *a priori* assumption.

4. *Adjectives Plus Nouns Plus Adverbs.*—Sixty words were combined in the following formations: "well kept houses," "very wealthy people," "little known articles," etc. The total median was thirteen; the uncategorial median, seven.

Comment.—According to grammarians (Jespersen,[12] Bréal[16] and Sapir,[18]) a noun like "widow" is very general, as it comprises all the widows existing. An adjective added to such a noun—"wealthy widow"—yields a more specific term, as there is only a restricted and therefore more specified number of wealthy widows. If an adverb is further added to the adjective—"very wealthy widow"—the specification is enhanced. On the other hand, the greater the degree of specification, the greater becomes the ease of handling a concept. But the result of the experiment was an uncategorial median of seven, hence a "failure."

5. *Verbs.*—Sixty verbs were given, ten infinitives—"to quit," "to be"—ten past tenses of regular verbs—"registered," "organized"—ten present tenses—"tells," "goes"—ten participles—"fleeing," "rising"—ten imperatives—"go," "hear"—and ten past tenses of irregular verbs—"lost," "torn." The total median was thirty-six; the uncategorial median, six.

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18. Sapir, E.: Language, New York, Harcourt, Brace & Company, 1921.

Comment.—The bulk of the mistakes was made in the infinitives ("speed" instead of "to speed"), in the past tenses of regular verbs ("register" for "registered"), in the present tenses ("go" for "goes") and in the participles ("flee" for "fleeing"). The imperatives ("go," "hear") and the past tenses of the irregular verbs ("lost," "torn") yielded a minimum of mistakes. As is readily seen, "grammatical" offenses were observed only when the grammatical distinction was expressed in the form of affixes ("flee-ing," "go-es"). When no affixes were given ("lost," "torn," "go"), only minimal mistakes occurred.

6. *Determined Plurals.*—Sixty combinations of words like "many houses," "several people," "six brothers," "much money," etc., were given. The total median was three; the uncategorial median, two.

Comment.—This test is in the nature of a crucial experiment. The arrangement is such that, once the first word of each word pair is pronounced, the singular or plural nature of the succeeding word is definitely determined. Thus, after the patient reads "many" no choice is left him but to follow up with a plural formation. Similarly, after the pronounciation of the word "much" no room is left but for a succeeding singular. The fact that in three separate performances not one confusion of plural and singular occurred was taken as undisputable evidence that the patient had a considerable facility for handling singular and plural, and that the mistakes observed in the preceding tests referred to a tendency to leave out affixes, not to an ignorance of "grammar."

7. *Particles.*—The patient was given sixty words like "at," "from," "where," "today," "another," etc. The total median was thirty-two; the uncategorial median, thirty-one.

Comment.—By particles is here understood any part of speech that does not fall under the heading of nouns, adjectives, verbs and numerals. In other words, they comprise pronouns, articles, prepositions, conjunctions, adverbs and auxiliary verbs. The test consisted of forty "short" particles like "at," "to," "as" and "in," and of twenty long particles, like "despite," "tomorrow" and "against." In tabulating the mistakes it was noted that of thirty-two mistakes encountered in one test, twenty-eight fell to the short particles and only four to the long particles. In order to get better insight into the patient's reaction toward the long particles, the following test was given.

8. *Long Particles.*—The patient was given sixty words like "beyond," "yesterday" "above" and "underneath." The total median was nineteen; the uncategorial median, nine.

Comment.—The conspicuous difference of the two tests in particles —an uncategorial median of nine in the one test as against one of

thirty-one in the other—proved definitely that the long particles were handled with greater ease than the short variety. It was now to be determined by the aid of new tests to what this difference was to be attributed. Two alternatives offered themselves for consideration. Most of the short particles consist either of two or of three letters. It was possible that the extreme shortness of the words was the reason for the failure. The other alternative was based on the fact that long and short particles differed radically with regard to their reference to meaning. Particles like "at," "as," etc., have practically no meaning of their own and acquire such meaning only when woven into context with other parts of speech. The meaningless word "at" acquires meaning in the combination "at home." On the other hand, particles like "beyond," "yesterday" have a definite meaning of their own, regardless of context. The question was: Were the short particles missed because of their shortness or because of their relative meaninglessness? To decide this question, the following tests were evolved.

9. *Short Meaningful Words.*—Sixty words consisting of three letters each like "son," "pin," "red," "cow," etc., were given. The total median was three; the uncategorial median, two.

Comment.—The ease of performing this test was so obvious that the element of shortness could be definitely discounted as a possible factor in determining the patient's attitude toward short particles. The following test was then devised to prove conclusively that the element of meaninglessness alone accounted for the failure.

10. *Short Meaningless Syllables.*—Sixty words, consisting of three letters each like "lem," "sim," "fik," "tek," etc., were given. The total median was forty-one, all, of course, being uncategorial.

Comment.—The fact that the patient was not able to handle meaningless material was conclusively evidenced by this test. The test, in addition, throws an interesting light on a further reaction of the patient toward meaningless material. Throughout there was a tendency to infuse meaning into the material. The syllable "sto" was read as "story," "fal" as "fat," "ser" as "serve," "tla" as "atlas," "cor" as "corrupt," "jun" as "jump," "lom" as "lemon," etc. A dual conclusion was drawn: (1) short particles were read defectively because they represented no sense; (2) when the patient encountered senseless material he tended to transform it into sense material.

11. *Figures and Abbreviations.*—Sixty words like "millions," "35 leaders," "five," "Dec. 27," "$5," "U. S.," etc., were given. The total median was twenty-eight; the uncategorial median, thirteen.

Comment.—That this test, with an uncategorial median of thirteen, presented a failure is evident. The problem of meaning was here

again brought out with great force. Figures, of themselves, have no meaning and gain such only in context with objects counted. Five men signify an assemblage of more than one man, but "5" in the abstract lacks significance. That abbreviations like "U. S.," "G. O. P.," "I. C." and signs like "$" have no direct but merely an underlying meaning to him who knows what underlies the symbols, goes without saying. The test, in other words, made the patient handle material which was devoid of or poor in meaning. The reaction was analogous to that observed in the test with meaningless monosyllabic words. Besides simple omissions and uncategorial substitutions, the mechanism of supplementing meaning was resorted to. Thus "1930 season" was read "Christmas season"; "two accidents" were transformed into "accidents occur"; out of "eighteen games" was made "eighteen games in row" (the patient was a moderate baseball and football fan). The words "first" and "ten years" stand close together in the test. They were transformed into the sequence "first years hardest." "Third quarter" was read as "quarterback."

12. *Isolated Letters and Abbreviations.*—This test, consisting of letters like A, P, C, k, h, etc., and of abbreviations like "Washington, D. C.," "John J. Peters," etc., did not lend itself to standardization on a sixty word basis. It contains thirty-three letters, both capitals and small letters, and thirty-two abbreviations. Of thirty-three letters, nine were missed. Of thirty-two abbreviations, again, nine were missed.

Comment.—A score of nine mistakes out of thirty-three or thirty-two constituted a definite failure. The tendency toward supplementing meaning was again in evidence. "J" was read as "John," "A. A. Low, M.D." was transformed into "Low, doctor medicine"; "William H. Taft" into "William Howard Taft."

13. *Particles in Context.*—Sixty words in combination like "from Heaven," "beyond repair," "what price glory," "off guard," "clear as mud," etc., were given.

Comment.—This test contained nineteen short and nine long particles. Of the nineteen short particles, seven were missed, and of the nine long particles, only one was missed. The result showed that when in their proper context both short and long particles yielded better performances. The element of meaning which is added by the context explains the improvement in performance.

B. SENTENCES

1. *Short Sentences Consisting of Subject and Predicate Only.*—The patient was given sixty words, arranged in sentences like "horses run," "birds fly," "women say," "people spend," etc. The total median was five; the uncategorial median, one.

Comment.—This test contains fifteen sentences of the type "horses run," and fifteen sentences of the type "women say." The sentence "horses run" has a well definable meaning. After it is pronounced, the statement is closed and calls for no supplementation. On the other hand, the sentence "women say" does not represent a closed proposition. After it is pronounced, it leaves open the question "what do women say?" The difference rests on the nature of the transitive versus the intransitive verb. An intransitive verb joined to a noun closes the proposition and demands no transition to an object, while a transitive verb demands such a transition to and supplementation by an object. The one is a "closed," the other an "open," sentence. Only a closed sentence has propositional meaning. An open sentence is merely a phrase but not a proposition, because it proposes nothing definite. On *a priori* grounds it was expected that the patient, who seemed to be oriented on meaning, would make more mistakes in the open sentences than in the closed propositions. The experiment again contradicted the *a priori* expectation.

2. *Closed Sentences, Consisting of Subject, Predicate and Object.*—Sixty word combinations like "France builds ships," "children play games," "waiters serve food," etc., were given. The total median was six; the uncategorial median, three.

3. *Nonsense Sentences Which Are Neither "Closed" Nor "Open."*—Sixty words identical with the sixty words of the preceding test, but in nonsense arrangement like "builds children games," "serve booksellers books," "make men wine," etc., were given. The total median was twenty-six; the uncategorial median, ten.

Comment.—With identically the same words the performance was "fair" in test 2 and "poor" in test 3. The patient's inability to manipulate nonsense material here again came to light prominently. A tendency to supplement meaning was again conspicuous. For instance, "play waiters food" was read "waiters sell food," "make stop listen" was read "stop look and listen."

4. *Closed Sentences in Which the Subject and the Predicate are Represented by Abstract Nouns.*—Sixty words arranged in propositions like, "honesty breeds confidence" and "distrust spoils friendship" were given. The total median was thirteen; the uncategorial median, four.

Comment.—Of interest was the patient's reaction to the nonsense variety of this test. The total median was twenty-one; the uncategorial median was two. In other words, with regard to uncategorial mistakes, the nonsense variety was managed with greater facility than the sense material. The reason why abstract words should be better treated in nonsense formations than concrete words I am unable to explain.

5. *Closed Sentences Consisting of Subject, Predicate and Adverb.*—Sixty words in sentences like "roses smell sweetly," "horses run fast," "children walk slowly," etc., were given. The total median was ten; the uncategorial median, two.

6. *Closed Sentences, Consisting of Subject, Predicate and Object, with Either Subject or Object or Both Composed of Two Words.*—Sixty words in sentences like "business men tell interesting stories," "little boys love adventure," "constant pain weakens sick people," etc., were given. The total median was fifteen; the uncategorial median, four. Of the nonsense variety, the total median was nineteen; the uncategorial median, eight.

7. *Closed Sentences Which Contain Particles.*—Sixty words in sentences like "executives receive greater salaries than employes," "soldiers are denied many comforts," "airplanes carry people across long distances," etc., were given. The total median was twenty-one; the uncategorial median, six. Of the nonsense variety, the total median was twenty-two; the uncategorial median, seven.

Comment.—In this test the patient had obviously reached the limit of his ability to manipulate closed sentences. Both in the sense and in the nonsense variety his median exceeded the limit of five uncategorial mistakes that was set for a "fair" performance. His "span" for closed sentences was therefore passed in this test.

8. *Closed Sentences Containing Particles and Figures.*—Sixty words in sentences like "every month has thirty days," "each year has 365 days," "a dozen contains twelve parts," etc., were given. The total median was fourteen; the uncategorial median, seven. Of the nonsense variety, the total median was thirty-one; the uncategorial median, thirteen.

Comment.—The poor result could be foreseen, as the test was "stuffed" with numerals and particles. However, the sentences were so constructed that the predicate followed the subject either as a self-evident explanation (every month—has thirty days) or as an actual definition (a dozen—contains twelve parts). It was thought that through this arrangement the test might prove more facile. The test, therefore, tended to investigate whether sentences which were known to exceed the patient's "span" could be made easier of performance through facilitation. The result was negative. The tendency to supplement meaning was again conspicuous.

9. *Closed Sentences in Which the Predicate Defines the Subject by Decomposing It into Its Verbal Components.*—Sixty words in sentences like "horseflesh is the flesh of horses," "watchmakers are the makers of watches," etc., were given. The total median was nineteen; the uncategorial median, sixteen.

Comment.—Two means were employed in this test to "facilitate" the performance: (1) the factor of definition, and (2) the expedient of repeating in the predicate the component parts of the subject (horseflesh—flesh of a horse). But through this maneuver two or three particles were introduced into the predicate and the facilitation naturally resulted in aggravation.

C. PARAGRAPH READING

1. Forty-three words[19] were given in two sentences which together formed one paragraph. The paragraph read as follows: Let us for once be honest about the pitiful part that the people—the common people—have actually played in the drama of cilivilization. Then we can take a good, deep breath of relief for the rather glorious part they are playing now. The total median was twenty-eight; the uncategorial median, twenty-four.

Nonsense variation: Pitiful of drama in people have let be actually that, etc. The total median was twenty-four; the uncategorial median, twenty-one.

The same test was then offered in vertical arrangement:

Let	part	played	take	rather
us	that	in	a	glorious
for	the	the	good	part
once	people	drama	deep	they
be	the	of	breath	are
honest	common	civilization	of	playing
about	people	then	relief	now.
the	have	we	for	
pitiful	actually	can	the	

The total median was seventeen; the uncategorial median, fourteen.

2. Sixty words were then given in the following paragraph: So far as wealth is concerned, America is probably the first nation on the face of the earth to realize the futility of amassing too much and to begin giving it away most lavishly when it acquired too much. There is hardly a rich man on this continent who is not putting his money back into the causes of common good.

Sense variation: The total median was thirty; the uncategorial median, twenty-four.

Nonsense variation: The total median was thirty-three; the uncategorial median, twenty.

Vertical variation: The total median was twenty-four; the uncategorial median, fifteen.

Comment.—That the reading of paragraphs would result in failure was to be anticipated since their structure requires the generous use of particles. But it was contrary to expectation that the nonsense variation should give a better uncategorial median than the sense variation. Equally surprising was it that the performance should improve when the paragraph was read in vertical arrangement. An attempt will be made to account for both phenomena in the discussion.

3. Paragraph reading in a foreign language was tested. Sixty words were taken from Cicero, De Oratore, liber primus: Cogitanti mihi, saepenumero et memoria vetera repetenti, perbeati fuisse, Quinte frater, illi videri solent, qui in optima republica, cum et honoribus, et rerum gestarum gloria florerent, eum vitae

19. In the beginning of this study the sixty word standard was not yet observed with sufficient strictness. The other reading tests in paragraphs followed the standard.

cursum tenere potuerunt, ut vel in negotio sine periculo, vel in otio cum dignitate esse possent. Ac fuit quidem, cum mihi quoque initium requiescendi, atque animum ad utriusque nostrum praeclara studia referendi.

Comment.—The result of this test was of considerable interest. No attempt was made to read the test as such. The words were either left out completely or replaced by corresponding symphonic English words. In this manner, "memoria" was converted into "memory," "vetera" into "vertebrae," "repetenti" into "repetition," "qui in" into "quinine," etc.

PRELIMINARY CONCLUSIONS AS TO THE PATIENT'S ABILITY TO MANAGE PARTS OF SPEECH, SENTENCES AND PARAGRAPHS

Measured by the number of uncategorial mistakes per sixty words, the median never exceeded four in any class of nouns. Hence, the performance was "fair" throughout. As to adjectives, the uncategorial median remained below five in the monosyllabic and bisyllabic series but rose to eight in the polysyllabic series. The residual efficiency, therefore, stopped at this stage of the performance. The "span" reached only to the bisyllabic series. The verbs were generally manipulated with a "fair" span as far as the roots were concerned. The insufficiency was brought out only in the verbal forms the roots of which were modified by affixes. Total failures were registered in particles, numerals, isolated letters and abbreviations. Sentences were still within the patient's span, even if they consisted of four or five words, provided they contained no particles or numerals. Even nonsense sentences remained within the span if the nouns which they contained consisted of abstracts. Paragraph reading was always a failure, the number of mistakes increasing proportionately in vertical, nonsense and sense arrangement. Paragraph reading in a sample of foreign language resulted in complete breakdown.

D. SUPPLEMENTARY PSYCHOLOGIC TESTS FOR READING

The foregoing reading tests had for their objective the measurement of the linguistic span. It now remained to apply analogous tests to the so-called psychologic span. To this effect, various tests were employed which are traditionally credited with the faculty of measuring such psychologic capacities as attention, concentration, categorization, correcting mistakes, discrimination, etc.

1. *Attention and Concentration.*—Bourdon's [20] cancellation test was applied in various arrangements. Series of long and short sentences were selected from the tests already described, both in their sense and in their nonsense varieties. The

20. Bourdon, B., quoted by Whipple, G. M.: Manual of Mental and Physical Tests, Baltimore, Warwick & York, Inc., 1910.

patient was then asked to cancel all a's, e's, b's and d's. Then he was directed to cancel two letters like a and e, b and d, and r and s. The result was similar to that noted by Bouman and Gruenbaum.[21] The nonsense material always yielded considerably fewer mistakes in considerably shorter time. Tests 7 and 8 of Jan. 18, 1930, represent a typical performance and will be given here in illustration. The patient was instructed to cancel a and e in the sequence of sentences "France builds ships," "children play games," etc. The series contains sixty-four a's and e's. The result was four mistakes in two minutes and forty-three seconds. The same letters were then canceled in the nonsense variation "builds children games," etc. The result was no mistakes in two minutes and twenty-five seconds. An analogous result was obtained with the cancellation of r and s. The sentence sequence chosen for this test was "roses smell sweetly," "horses run fast," etc. The series contained sixty-three r's and s's. The score was twelve mistakes in three minutes and sixteen seconds for the sense variation and five mistakes in three minutes and four seconds for the nonsense variation.

Comment.—The patient's attitude toward sense and nonsense material was exactly the reverse of that which was observed in the corresponding linguistic group of reading tests. There he had found more difficulty with nonsense material, here the difficulty was increased in sense material. Apart from this attitude, the tests proved that the patient was well able to concentrate attention on a given task of moderate complexity. The inference seemed justified that his defective performances in reading aloud were not due to an inability to concentrate his attention on a task.

2. *Discrimination.*—The patient was given sixty words containing twelve names for colors (green, red, etc.), twelve names for fruits (peaches, prunes, etc.), twelve names for metals (iron, copper, etc.), twelve names for trees (pine, fir, etc.) and twelve names for animals (dog, cat, etc.). All the metals of the series had to be underscored. The patient made one mistake, leaving out "nickel." The same sixty words were given on another day with the direction to read the individual words and to name the class (color, fruit, metal, tree or animal) to which each belonged. The result was six mistakes. "Poplar" was designated as an animal, "beech" as a fruit, "fox" as a tree and "grapefruit," "lilac" and "zinc" were omitted.

He was then given sixty words, containing thirty words allied to hatred and thirty words allied to love, and asked to underscore all the words related to hatred. The "hatred" series consisted of words like "anger," "animosity," "malice," "dislike," etc.; the "love" series consisted of words like "affection," "fondness," "friendship," "gentleness," etc. The score was five mistakes. "Pity," "amity" and "alliance" were underscored; "argument" and "gloom" were omitted.

Comment.—The three tests showed that the patient's power of discrimination was by no means considerably below the norm. The conclusion seemed warranted that his "grammatical" defects could not be ascribed to any lack of discrimination.

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21. Bouman, A., and Gruenbaum, A. A.: Experimentell-psychologische Untersuchungen zur Aphasie und Paraphasie, Ztschr. f. d. ges. Neurol. u. Psychiat. **96**:481, 1925.

3. *Correcting Misprints.*—The patient was given a series of closed sentences consisting partly of misprinted and partly of correctly printed words. He was directed to underscore words that he thought contained mistakes. The sentences read as follows: "Fiedship bings haphiness," "genrals need amies," "itt rains," "hee laughs," etc. Five mistakes were overlooked in "peple," "killd," "cigart," "citys" and "citzen." None of the correctly spelled words was underscored.

Comment.—This test, it was thought, proved that the patient had a fair visual conception of the picture of words. A potential word blindness, therefore, could not be made responsible for his "grammatical" defects.

4. *Correcting Ungrammatical Material.*—Sentences and word combinations were given, containing sixty words in which the particles were omitted. The patient was instructed to correct the mistakes. The test read as follows: "Rain falls —— clouds," "people sleep —— beds," "spitting —— floor —— prohibited," etc. A total of fifteen particles had to be inserted; three were missed.

Another series with faulty conjugation and with defective plurals and singulars was then given with the instruction to correct the mistakes. The material, containing sixty words, read as follows: "heavy rain falled," "children cries," "teared pants," "shoes portect foots," etc. Only one mistake was overlooked, all the others being corrected.

Comment.—The first of these two tests shows that the patient, as is already known, is fairly well able to supplement meaning. The second test proves that real grammatical mistakes, in contradistinction to affix structures, challenge the patient's sense for grammatical meaning and are promptly corrected.

5. *Response to Nongrammatical Nonsense.*—Sixty words, arranged in sentences like "crooks deserve confidence," "fools possess wisdom," "streetcars dream," "apples sneeze," etc., were given. The total median was two; the uncategorial median, two.

Comment.—This test consists of closed sentences and is, therefore, sense material from a grammatical point of view. But from the standpoint of common experience and logic each sentence contains an absurdity. The object was to find out how the patient would react to material which, conforming to grammatical meaning, offended empiric and logical meaning. It was proved that the type of meaning the patient was focused on did not coincide with empiric or logical meaning, but purely with grammatical meaning. Grammatical meaning, in contrast to logical and empiric meaning, does not depend on the substance and contents of a proposition, but merely on its formal structure.

SUMMARY OF THE RESULTS OBTAINED FROM THE PSYCHOLOGIC SERIES OF THE READING TESTS

The patient was shown to have a fair control of attention and concentration. His powers of discrimination between material categories

(colors, fruits, trees, etc.) and emotional categories (concepts related to hatred and love) were preserved to a considerable degree. He was well able to correct mistakes in grammar and spelling. Finally, it was demonstrated that the type of meaning which was so prominent a factor in his disturbance was purely grammatical, not empiric.

SILENT READING

1. *Single Letters.*—The letters of the alphabet were gummed singly on small pieces of cardboard and all the letters shuffled, i.e., thrown on the table in disorder. The patient was then asked to reshuffle the letters and to put them in alphabetical order. After two minutes he managed to arrange A, B and C in due order, but then he became totally helpless. He was then given parts of the alphabet, e. g., the letters A to F, A to H, etc., in disordered array. When asked to reshuffle, he was never able to get beyond the D in alphabetical order. When he had disarranged the letters like A B C E D F I G K and was then asked whether the arrangement was correct, he generally answered with a "yes."

The letters A B C D E F G were then placed on the table in alphabetical order, left exposed for a short time and shuffled. Now he reshuffled them correctly in fifty seconds. On a second repetition, he reshuffled correctly in forty seconds; the third time in thirty-five seconds, but in the order: A B E C D F G. When checked, he corrected promptly.

He was then given the letters P Y X S M N U F B R and asked to pick out the letter R. He first picked M, then R. After the first mistake, various other letters were picked promptly.

The letters K L V Q Z were then added to the former batch and the patient directed to pick the R from the whole pile of fifteen letters. He did so after thirty seconds. Other letters were picked promptly in considerably less time.

Comment.—Simple as this test appears to be, it is in fact of a very high complexity. The complexity is due mainly to the relatively involved nature of the "order." In the tests for reading aloud the order was uniformly: "read." Now it was changed into a sequence of sentences. The patient was, for instance, told: "Here are letters. I shall throw them on the table. Put them together in alphabetical order." The question was whether the patient would be able to "grasp" the essential point, and whether he would keep the order and its essential point in mind. His ability both to accept and to retain the order was evidenced by the fact that even after wrong performances he could repeat the order correctly.

The task of arranging letters in alphabetical order involves a kind of mental activity totally different from that of picking out single letters from a pile of letters. In the former task it is a matter of arranging elements which, in themselves, are meaningless (letters) into a meaningful, well ordered whole (alphabet). In the latter task it is merely a question of recognizing the letter demanded. Recognizing letters is identical with reading them silently. So this task involved merely an order to read. But in the former task the patient had first to read or recognize the individual letters, then to arrange them into a mean-

ingful whole (alphabet). The test which, periodically repeated, always gave analogous results showed that the patient was merely able to construct simple wholes (A B C D). Beyond D he invariably failed. When a whole, comprising more than four parts—A B C D E F G—was first exposed to view and then shuffled, he was able to rearrange it in the required structural order. The visual aid apparently facilitated the performance. The "span," therefore, was four letters on plain order and seven letters with visual facilitation.

2. *Monosyllabic Words.*—The letters B E D were placed on the table and arranged into BED. Then the three letters were shuffled and the patient asked to reshuffle them. This he did promptly. CORN, PLAY, NEW, YORK, TURN, RIGHT, etc., were also reshuffled correctly after they had been exposed. But when two words together—BED CORN; NEW YORK; TURN RIGHT—were exposed and shuffled, the reshuffling was impossible. Words containing more than four letters, e. g., CIGAR, were never reshuffled.

Comment.—This test is analogous to the preceding test. It required, beside silent reading, the rearrangement of meaningless elements into a meaningful whole. The "span" was passed in single words containing more than four letters.

3. *Sentences.*—The words, "France," "builds" and "ships," gummed singly on cardboard, were thrown on the table and the patient asked to form a sentence out of the three words. This was done promptly. "Waiters," "serve" and "food" were rearranged with equal promptness. Then, all the six words were thrown on the table and rearranged correctly. The patient performed equally well with three other sentences, containing nine words. When the fifteen words were thrown on the table, they were again promptly rearranged in their sentential order.

In the sentence series "roses smell sweetly" and "meat spoils easily," he made several initial mistakes, but corrected them easily.

In the series with four or five words, like "business men tell interesting stories," he performed with fair success, but the mistakes grew more numerous.

The sentences that contained one particle, like "executives receive greater salaries than employes," were poorly handled. When he was given the sentence series with two or more particles, like "cigar makers are the makers of cigars" (definitions), he failed completely and exclaimed characteristically: "it got me here," indicating that he had definitely exceeded his "span."

Comment.—In this test the patient had to construct sentences out of words. This involved the building up of more advanced wholes (sentences) out of primitive wholes (words). He performed satisfactorily until particles entered into the task. Particles, having no meaning of their own, form not even a primitive meaningful whole. The "span" was reached when they were introduced.

WRITING

1. *Writing from Copy.*—The patient had received instruction in writing with his left hand and was able to copy any kind of material, sense and nonsense, letters, words, sentences and paragraphs, both from print and from cursive hand-

writing. The average was from eighteen to twenty letters per minute. He never copied one word in continuity. He "painted" letter after letter.

2. *Writing from Exposure.*—The material was exposed for a few seconds, then withdrawn from view and the patient directed to write down what was shown him. (*a*) Letters: they were well handled without exception. (*b*) Parts of speech: the patient was shown each twenty nouns, adjectives, verbs, particles, etc., and asked to write them down after a short exposure. Whether it was nouns, adjectives, particles or nonsense material, he was able to write them down, if they consisted of three or four letters only. At the fifth letter he always failed. For instance, he was able to write "son," "dry," "big," "sure," "who," "where," "lost" and "card." But when given the word "tomorrow," he would write "tomor" and then stop or, when checked, would add some uncorrelated letters like "tomor-ey." A similar observation was made with figures. A figure consisting of one or two numerals was written correctly. With three numerals he began having difficulties and made mistakes, except in figures which contained zeros as 100, 1,000, 150. (*c*) Sentences: sentences proved a complete failure, in full accord with the fact that words containing more than four letters could not be written.

3. *Writing from Dictation.*—This proved a failure throughout; the relatively best performance was obtained in letters. But even these were often missed. Words with more than three letters were never written correctly; words with only three letters, sometimes. Among the numerals the units (1 to 10) were handled well, but the tens and hundreds were totally bungled.

Comment.—Spoken language can be acquired without any special instruction, by mere listening and imitation. Primitive reading, of shop signs for instance, can also be acquired spontaneously. But writing requires special training. Being a relatively late acquisition, it is one of the functions which, according to Pitres'[22] law, comes late in the process of restitution. That the performance was best in copying, less good in writing from exposure and worst in writing from dictation merely emphasizes the fact that the patient could much more easily make use of vision than of audition, as an aid to performance.

REPEATING

1. *Words.*—Whether long or short, sense or nonsense, words were always repeated correctly.

2. *Sentences.*—Closed sentences, like "babies cry," "doctors prescribe medicine," etc., were handled with great accuracy. Equally accurate were the performances with compound closed sentences like "the king builds a palace, and the palace has electricity." The difficulty began with sentences which contained particles. "The doctor lives uptown" was repeated correctly, also "the doctor has his office downtown." But the compound sentence "the doctor lives uptown and has his office downtown" was bungled completely.

Comment.—To repeat a word means to reproduce the acoustic impression left in the ear. This is more or less a mechanical per-

22. Pitres, A.: Étude sur l'aphasie, Rev. méd. **15**:873 (Nov.) 1895.

formance. A mistake is hardly possible except in a case of word deafness. To repeat a sentence like "the doctor prescribes medicine" already leaves room for confusion. The repetition could run: "medicine prescribes doctors" or "describe" could be substituted for "prescribe." Such mistakes can be avoided only if the patient keeps in mind not only the words but also the thought expressed. The realm of the mechanical is here passed and the region of the mental entered. The patient has now to keep in mind, not only a mere aggregate of words but words arranged in a "Gestalt." But the "Gestalt" is of a simple nature and well within the "span" of the patient. Even such relatively complex "Gestalten" as "the king is tall, and his palace is marvellous" are still within the "span." But in the sequence of sentences "the doctor lives uptown, and his office is downtown" the "span" is obviously passed.

PRAXIA

Marie's[23] tests with the paper slips, chair and window were performed correctly. The orders were then complicated. The patient was asked to go to the door, to open it, to close it again and to shut off the radiator. The performance was correct. He was then instructed to take four paper clips out of a clip container, to put two on top of a lamp shade and to throw two into the waste basket. Execution was correct. When asked to look up the tenth line on page 200 of a book, he performed slowly but correctly.

He was able to make a fist, to whistle, to threaten, to indicate "yes" and "no" with his head, to bend the arm, to stretch out the leg and to button and unbutton his coat. But in orders involving the understanding of particles he began making mistakes. The order "put the pen on the ashtray" was carried out. But the order "give it to me" was missed. The pen was put on the table. Even when specified in the form "give me the pen" it was impossible of execution.

He was told: "Here are four things, pencil, watch, ashtray and paper. Put the pencil between the ashtray and the paper." He took the pencil in his hand and put the paper beside the watch. He was unable to hold, on order, a match underneath the table or to hold a pencil above the table. But when asked to hold the pencil above his head or below his chin, or to put the watch on his nose or to hold it between his eyes, he performed well.

Right and left were almost constantly missed. The few correct performances could be credited to the 50 per cent chance factor implied in the nature of the performance.

The following orders were typewritten on pieces of cardboard: "close eyes," "open mouth," "touch nose," "close window," "open door," "pull shade," "make fist," "clear throat." The performance was good.

Orders containing one particle were still performed, e. g., "place arm on table," "put arm in pocket," "put hand to eye" and "touch teeth with fingers." But the orders containing two particles like "pull pen from the penholder" and "open button of the coat" were not performed.

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23. Marie, P.: Révision de la question de l'aphasie, Semaine méd. **26**:241 (May 23) 1906.

Orders containing pronouns were performed when the act referred to his own body, e. g., "show your nose," "open your coat" and "raise your leg." But when the pronoun referred to my person, the order was missed, e. g., "touch my chair, my hand," "grab my arm," etc.

Comment.—The patient was eupraxic even in such complex orders as to look up the tenth line of a given page in a given book. But the order "give me the pen" met with complete failure. Failure was also registered in orders involving prepositions like "above," "below," "beside," etc. Reduced to the terms of "Gestalt" thinking, he was able to carry out complex orders, provided they had no reference to space—"Gestalten." But when spatial orientation was a factor, even simple performances were missed. Pronouns like "me," "you," etc., obviously refer to this spatial element. The "span" of his spatial orientation was exceeded the moment the patient had to go beyond the sphere of his own body. Thus, he was able to carry out the order "hold the pencil above your head," "below your chin" or "hold the watch between your eyes"; but he was unable to execute the order "hold the match underneath the table," or "give me the pen." The relation between himself and the watch he understood. But of the relation between the watch and the table or between the pen and me he seemed to have no conception.

ARITHMETICAL OPERATIONS

1. *Arithmetical Manipulation of Objects.*—The patient was given one quarter, three dimes and three nickels and asked to hand me half a dollar. He picked one quarter, two dimes and one nickel. The operation was repeatedly correct with most combinations of coins below one dollar. With combinations above one dollar, he made frequent mistakes.

He was then given a pile of eleven paper clips. (How many are they?) [24] Eleven. (Take out three). Correct. (Put two clips to the three). Correct. (How many are they together?) Five. (Put another four to them). Correct. (How many are they now?) Nine. Many other additions of this kind were executed correctly. But the handling of more than fifteen clips met with great difficulty.

He was asked: "How many are five clips and six clips together?" He answered: Six. Then he was asked to pick first five clips from a pile, then six clips. (How many are they together?) Eleven.

Three rubber bands were placed on the table, 5 inches apart from each other. He was asked to put five clips to each rubber band. (How many rubbers?) Three. (How many clips?) Fifteen. Beyond the figure fifteen he again fumbled repeatedly.

He was given eighteen clips and asked to arrange them in one row. He did so correctly. Then he was asked to pick the sixth, tenth and fourteenth clip. He performed correctly.

He was given fifteen clips and asked to distribute them in equal parts to the three rubbers. He was helpless in spite of frequent explanations.

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24. The parenthetical sentences contain the questions and orders of the examiner.

He counted a pile of eighteen clips correctly. He was then asked to take seven clips from the pile. He was unable to tell how many were left.

2. *Quantitative Valuation of Numerical Concepts.*—He was asked to tell the price of a coat and a tie, of a horse and a chicken, of a package of cigarets and a carton of cigarets, etc. He named approximately correct figures. When big figures were involved, as for instance the price of a bungalow, he said: "I can't say it but I can write it." He then wrote 2,500 and said: "Two fifty five."

He was able to name the number of days in a week or in a year, the number of weeks in a year, a month, etc.

When asked the following questions: "What is longer, an hour or a day, a week or a month?" he made frequent mistakes. He was also unable to state correctly what was bigger, more, etc., in questions pertaining to yard and foot, ounce and pint, thirty-six and thirty-seven and other figures. But questions pertaining to the difference of size or age between father and son, grandfather and father, house and bungalow, etc., were well answered.

He was told: "The United States have one hundred million population. New York State has ten million population. Which of the two is bigger?" He was unable to answer.

3. *Silent Reading of Numbers.*—A square, 7 by 9 inches, was divided, chessboard-like into sixty-three fields. The figures one to forty-seven were so inserted into the fields that four small squares were left vacant in each corner, giving the whole the arrangement of a cross. The patient was then asked to touch with a wooden applicator all the figures which contained a five or a multiple of five. After due explanation of the task he picked 5, 10, 20, 25, 30, 35, 40, 45, leaving out 15. He was then asked to point with his finger to 3, 29, 18, etc. He made no mistake.

When he was asked to show the figure that stands before 19, after 19, between 2 and 3, etc., he failed completely.

He was given a calendar, containing all the months of 1930, and asked: "On what day falls January 13, February 25, July 17?" He found the names of the days correctly.

4. *Handling of Figures Outside Their Visual or Objective Context.*—He counted correctly from 13 to 24, then left out 25 and continued 26, 27, etc. Backward counting was very deficient.

He was unable to tell what figure came before 20, after 8, etc.

I told him: "I shall count and when I make a mistake you must check me." I then counted: 27, 26, 25, 24, 23, 20. He checked me and said: 22.

I told him: "Keep the figure 625 in mind. I shall call several figures and when I come to the figure 625, you must stop me." I then said: 46, 360, 630, 808, 25, 629, 87, 625. He said: "That's it." On various repetitions of this test he made numerous mistakes, but quite often hit the right number.

5. *Handling of Arithmetical Operations in Writing.*—I wrote various figures below each other and asked him to do the sum.

I put down:	2	12	19	25	18	37	98	125
	5	15	13	17	97	58	18	234
	—	—	—	—	—	—	—	—
He summed up	7	27	31	42	..	95	10–5	...

In the figures in which he had to carry over a numeral, he put down the tens first, then the units (10-5).

6. *Mental Arithmetic.*—He was helpless throughout in additions, subtractions, multiplications and divisions of the simplest order. When he was asked: "How much is thirteen minus nine?" he said: "I can't spell minus." I then asked: "How much is thirteen less nine?" He answered: "I can't spell that either."

Comment.—If a pile of clips is declared to be equivalent to the figure 6, it is counted. If several piles are counted and combined, the process is one of addition or multiplication. If one large pile is counted and then decomposed into its parts, the process involves subtraction or division. Addition and multiplication combine primitive parts into a primitive whole. They synthesize magnitudes. Subtraction and division, on the other hand, decompose a given whole into its parts and thus analyze it. The tests showed that the patient was able to handle small piles of objects by way of addition and multiplication and failed completely in the task of subtracting and dividing piles. In other words, his span was fair in matters of synthesizing parts into a whole, but practically abolished in matters of analyzing a whole into its parts. In the quantitative comparison of objects of experience—coat and tie, horse and chicken, year and month—his span was fair. But it was definitely exceeded when he was to compare abstract figures of more than 2 numerals. He also failed when he had to compare objects which represented large figures—100,000,000 population of the United States with 10,000,000 population of New York State. In the silent reading of numbers his span was fair, even good. But in mental arithmetic it was absolutely nil; in carrying out arithmetical operations on paper it was rather poor, and in handling figures without visual or objective context, the span was definitely reduced.

TIME PERCEPTION

The patient was unable to tell which day came after Monday, before Monday; which year after 1922.

I told him: "We have now 1930. Which was the last year?" He said: twenty-nine. He was then unable to say which was the year before 1929.

He almost always read the time from the watch correctly. In his answers he always said four thirty; five fifteen, never half past four or a quarter to six.

He was asked to arrange the minute and second hands of my watch so that they showed successively 12 o'clock, 4 o'clock, 5:15, 6:45, etc. He always performed promptly. But when asked to put them at a quarter past four, at half past six, etc., he invariably failed. He was able to tell how much time it took to travel from his home downtown, from Chicago to New York and from Chicago to Europe.

Tapping rhythms (von Woerkom[25]): I tapped the table with my fingers, producing iambic rhythms (⏑–⏑–), trochees (–⏑–⏑), dactyls (–⏑⏑–⏑⏑), anapests (⏑⏑–⏑⏑–) and various other combinations of accented and unaccented taps. He promptly repeated them with his fingers.

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25. von Woerkom, W.: Sur l'état psychique des aphasiques, Encéphale **18**: 286 (May) 1923; Ueber Stoerungen im Denken bei Aphasie-Patienten, Monatschr. f. Psychiat. u. Neurol. **59**:256, 1925.

Comment.—A correct estimate of time presupposes a proper conception of sequence and antecedence and a sufficient perception of rhythm. The tests showed that the patient's sense of rhythm covered the normal span, but that his span for perceiving sequences and antecedences was practically zero. If the perception of time was linked up with objective experience (description of distances between two towns or two continents), his span was fair.

SPATIAL ORIENTATION

The patient's lack of orientation with regard to right and left and with regard to prepositions was amply illustrated in the tests for praxia.

1. *Spatial Orientation Without the Verbal Use of Prepositions.*—Three clips were put on the table, the first about 10 inches from the second, the second about 3 inches from the third. The patient was then asked to arrange the clips at equal distances from each other. This he did promptly. The three clips were then placed on a sheet of paper, the first in the right upper corner, the second in the left lower corner. The patient had to place the third clip so that it was in line with and at equal distance from the two other clips. He did so promptly.

He was shown a brown, red and black pencil with the red pencil placed between the two others. The pencils were left exposed for a few seconds. Then they were disarranged. He rearranged them in their original order.

The black pencil was then placed obliquely to the others. After short exposure they were disarranged, whereupon he rearranged them promptly.

He was shown a square, formed of four clips. After exposure and disarrangement he rearranged the square. Equally good performances were furnished with oblongs, double squares, triangles, etc.

2. *Abstract Perception of Space.*—A line, 10 inches long, was drawn on a sheet of paper. The patient was unable to indicate the middle of the line. I then divided it into two unequal parts. He showed the bigger and smaller part. When the line was divided into four unequal parts he was able to indicate, as directed, the smallest, biggest, second biggest and third biggest portion without mistake.

He was shown two circles which intersected. He was unable to indicate the points where they intersected.

He was shown a sheet of paper with vertical and horizontal lines arranged in gridiron form. I told him: "A man moves downward along this vertical line, and another man moves along on this horizontal line. Where will they meet?" He was helpless.

3. *Spatial Memory.*—He knew the street where he had lived but not the number of the house. When asked how he would reach downtown from where he lived, he gave a correct answer (Halsted street car). He did not know which street was farther north, Chicago Avenue or North Avenue.

He was asked: "Where is the Foreman Bank?" He said: Downtown. (Is it on Franklin Street?) No. (On Dearborn Street?) No. (On Polk Street?) No. (On LaSalle Street?) No. (On State Street?) No. (On Clark Street?) Yes. (Are you sure?) No.

He was asked: "How many miles is it from Chicago to Milwaukee?" He took a pencil and said: I can explain it. Then he wrote 85 and read 65. (How many miles from Chicago to New York?) Ten hundred miles.

Comment.—The patient was able to arrange and rearrange objects in their proper spatial order. His handling of spatial symbols (straight lines, circles, etc.) was somewhat defective. He failed in tasks that required an adequate memory for space. His inability to orient himself spatially in response to questions containing prepositions and right and left concepts had already been brought out in the tests for praxia.

MISCELLANEOUS TESTS FOR HANDLING GRAMMAR AND SYNTAX

1. *Correcting Mistakes.—(a)* Plural and Singular: Defective formations were offered in speech, like "seven woman," "five child," "twenty day," "several ox," "many animal," etc. He corrected them promptly, even correcting "seven woman" into "seven women" by his mode of pronunciation.

(*b*) Tenses: Sentences were given, like "I writed a letter," "I buyed a watch," etc. Correction was prompt.

When he was asked: "Do you say: Yesterday I shall take a walk?" or: Tomorrow I took a walk," etc., he made many mistakes.

(*c*) Passive voice: He was told: I threw somebody down the stairs. What happened to him? He answered: He falls. To the question: If I throw a stone, what happens to the stone? He replied: It throws. I then said: You must answer: The stone is thrown. Then he understood and converted the following sentences from the active into the passive voice: "I spank a child," e. g., was converted into: "He is spanked," etc.

(*d*) Prepositional Sentences: Sentences like "I sleep from the bed," "I sit from the chair," etc., were converted into: "I sleep on the bed," "I sit on the chair," etc. However, numerous mistakes were made.

2. *Relation of the Sentence and Its Parts.*—He was told the sentence: "France builds ships" and asked: Who builds? Answer: France. (What does France do?) Builds ships. (What does it build?) Ships. He was then asked analogous questions concerning the sentence: Important sales begin tomorrow. He assigned to every word its proper place and functions.

3. *Forming Sentences After a Given Pattern.*—He was told: Form a sentence like: I have a dog. He said: I have a watch. I have a book. I have a book by Charles Darwin. I have a tie. I have a collar. I have a vest. I have a shirt. I have slippers. I have some socks.

Then he was asked to form sentences like: The city of Chicago has streets. He said: The city of Chicago has block streets. It has asphalt streets. It has concrete mixtures. It has incinerators.

Comment.—The performance was fair in the task of correcting mistakes and of assigning the parts their proper position within the sentence. But the prepositional mistakes were only partly corrected. The formation of sentences after patterns was satisfactory as to form but poor as to content. Once he was started on a sentence like: "I have a tie," he continued monotonously in the same sphere of objects (coat, vest, shirt, slippers, etc.). This behavior corresponds to what is called in German "haftenbleiben."

APPERCEPTION

1. *Formal Apperception, Without Regard to Meaning.*—(*a*) Spelling: The patient was given typewritten and printed words and asked to spell them from sight. "France" was spelled F-r-a; "hunters" h-u-n; "doctors" d-a; "shoemakers" s-h. In mental spelling without visual aid, he was not even able to spell the first two letters of a word, sometimes not even the first letter. Even my name which he was able to handle in writing to dictation he could not spell. He said: L-o.

(*b*) Indicating the Number of Syllables, After Lichtheim:[26] There was complete failure with monosyllabic, bisyllabic and polysyllabic words.

(*c*) Grouping of Words on the Basis of Assonance: He was asked to name words which begin with A. He said: aunt, as, is and have. Words which begin with G: Good husbands—husbands—good—.

2. *Apperception of Context and Meaning.*—(*a*) Primitive Apperception of Meaning: He was able to describe from memory the color of objects, e.g., peach (red); currants (yellow); milk (white), etc. But he was very defective in the description of shape. When asked how a church looked, he said: I don't know but I can draw it. He then drew a structure with a spire and cross that recalled the shape of a church. A horse he described: Four foot—a tail—teeth—that's all. The shape of an elephant he was unable to describe, but drew it fairly well. When asked to describe the shape of a peach, he said: It is yellow and red. When I told him I wanted the shape, he was helpless. I then showed him my watch and said: This is round and flat. How is a peach? He answered: It is red and yellow—it is round.

On request he drew a peach, a pear, a cherry, a circle, a house and a box. The latter was drawn stereoscopically, the other objects bidimensionally, all of them fairly well.

(b) Apperception of Complex (Intellectual) Meaning: He was told: A man started a hotel. He is not yet in the directory. How will you talk to him by telephone? He said: I'll call him up. (How will you do that?) I'll get his number. (What will you do to get his number?) I'll try to get it. (Who can give it to you?) The operator. (Which operator?) Long distance. (Which operator will you ask for?) ———.

He was asked: If you want to call me up, what will you do? He said: I'll get your number. (How will you get it?) Put a nickel in the slot—ten cents—and ask for Dr. Low.

The question was put to him: If you have a flat tire on the road, how will you fix it? He said: I'll put a pair of overalls on and patch it up with cement. (What will you do then?) Jack it up and go ahead.

(*c*) Apperception of Complex (Emotional) Meaning: I told him: A driver whips his horse so that blood comes. What do you think about that? Well, he said, mistreat. (What do you think about the driver?) Well, he could be drunk. (But if he isn't drunk?) Inhumanity to horses.

I said: A man jumps into the river to save a boy from drowning. How would you call him? He said: Hero. (How should the rescued boy be?) Flat on the ground to get the water out of his lungs. (How should he feel toward the man?) He should feel that he saved the boy's life. (Is that all?) Well—he should be thankful.

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26. Lichtheim, L.: Ueber Aphasie, Arch. f. klin. Med. **36**:204, 1885.

I told him: I'll make a European trip, and there will be a storm on the ocean. How will I feel? He said: Well, it's kind of windy. You'll have to get under cover. (But if the boat is damaged?) Fear. I continued: On my trip I shall see beautiful churches and palaces. How will I feel about that? He answered: Well, there is no king in America. (Will I get sore at them?) No. (How will I feel about them?) ———

Comment.—To see a table, to touch it, to hear its thud when impacting on the floor is to perceive the object through the senses. This is called sense perception. If now the percept "table" is grouped under the category "office equipment" or "dining room furniture," something has been added to the process of perception and instead of being merely perceived the table has been ad-perceived or ap-perceived. In other words, a category, added to perception, yields apperception. Now, there are "tables" and "chairs" and "couches" in reality. But nowhere in reality is to be found "furniture" or "equipment." Given one table, six chairs, one couch, two curtains and one carpet, the senses will perceive only eleven "objects." If you now add that these eleven objects are used for the purpose of transacting business, you no longer deal with eleven separate objects, but with one unit of "office equipment." Should you decide to make use of the eleven pieces for the purpose of assembling the family for common meals, you would transform them into the unit "dining room." In either event you have grouped a manifold of particulate objects under the unifying category of use and purpose. Use and purpose have no actual existence in objective reality. They are merely mental entities, categories under which existing things are apperceived. In other words, objective reality offers perceptions, and the mind thinks of them or apperceives them, e. g., under the categories of use and purpose.

In the sentence "a driver whips his horse so that blood flows," the patient is presented with the four perceptions "driver," "whip," "horse" and "flow of blood." Now he is asked to apperceive the manifold of perceptions under one unifying category. Apperception is effected either through intellectual (contemplative) categories or through emotional (affective) categories. If one merely watches and observes the act of a driver whipping his horse, one applies his intellect (perhaps solely for the purpose of exercising it) and reflects on the strength of the driver, the resistance of the horse, the amount of blood that can be withdrawn without the horse collapsing, etc. One has, then, apperceived the manifold of perceptions under the categories of physics or physiology. These categories are impersonal, matter-of-fact, contemplative. But if one apperceives the process under emotional and personal categories, one may either enjoy the spectacle and apperceive it under the specific emotional category of "sadism." Or he may apperceive it under the category of "pity" and experience pain. Apperceiving by means of the

category "injustice" and "brutality," one becomes aroused to anger and indignation. The same act may be brought under different apperceptive categories. If a man is able to shift his modes of apperception from one category to another, he shows a control of numerous categories and is said to possess a "wealth of imagination." (Note that imagination is the popular name for apperception.) If the shift is effected with reasonable swiftness, the imagination is said to be alert.

The patient, presented with the picture of the brutal driver, applied the category "mistreating" to the situation. When checked, he shifted his apperception to the category "drunkenness." Finally, he reached the term "inhumanity to horses." His apperceptive processes were certainly reduced in wealth and alertness. This poverty and dulness of the apperceptive faculties came into even greater prominence in the instance of the drowning boy being saved by an intrepid man. The patient always remained the disinterested, impersonal observer. The boy should lie "flat on the ground to get the water out of his lungs." Only after long hesitation did it occur to his imagination that the boy should be thankful. My reaction to a storm on the ocean he summed up in the totally unemotional estimate that it would be "kind of windy" and I would have "to run for cover." With regard to my visiting magnificent churches and palaces his surmise was that Europeans were monarchical and Americans republican. All in all, his apperception was focused almost exclusively on matter-of-fact, impersonal categories. Emotional categories seemed hardly to enter the fabric of his apperceptive judgment.

Apperception proceeds either from the manifold of sense experience to categorial unification or vice versa. Presented with the sentence "a driver whips, etc.," one is given a fourfold of sense experience and required to synthesize it under one category. This involves a process of apperceptive synthesis. On the other hand, when asked the question: How does a horse look? one is given a whole which is already synthesized (horse) and required to analyze it into its manifold constituents. This involved a process of apperceptive analysis and resulted in failure. When the patient was asked to describe the color of a peach, the task was to isolate or analyze the detail "red" out of the totality "peach." This primitive act of apperceptive analysis was well within his span. But the shape of the peach he could not describe. Without going into lengthy disquisitions, it may be stated that in order to isolate the detail "red" from the apperceptive total "peach," the patient had only to recall one sense perception, namely, sight. But in order to recall the detail "round," he had to reproduce perceptions referring to the sphere of sight and touch. This double analysis seemed to surpass his span. That he was unable to describe but able to draw a church is in perfect agreement with this explanation. In drawing he made use of visual percep-

tions only. The manner in which he described the horse was interesting. The only details that were singled out for analysis were the four feet, the tail and the teeth. This description fitted practically every mammal. The characteristic details, like the mane, the erect ears, the delicacy of the legs and ankles, the long, straight neck, etc., were omitted from the description. He missed the distinctive "points." It is apperception that, in a narrative or any mental activity, makes one "stick to the point."

A complete failure was registered when the patient was asked to describe how he would effect a telephone conversation with the man who had started a hotel and was not yet listed in the directory. What he was expected to do was to analyze the total of the telephone talk into the details of putting a nickel in the slot, asking for information, receiving the new number, calling the operator again, etc. Instead he merely said: "I'll call him up" or "I'll get his number." What he did was to substitute one total for another. In the instance with the flat tire, a few details were mentioned, but they were too comprehensive and not "detailed" enough. They could hardly be called analytic.

The inability to spell a word or to name the number of its syllables or to name words that begin with A or G falls under the same heading of defective analysis. In spelling, the total of a word must be analyzed into its parts. The same applies to syllabization where the word must be analyzed into its syllables. That the task of naming words that begin with a given letter requires an analytic act needs no explanation.

Summing up, the patient showed a capacity to bring perceptions synthetically under apperceptive categories, but the categories were of the matter-of-fact or intellectual type. The emotional variety of apperceptive synthesis was beyond his span. In the domain of analytic apperception he was able to isolate a detail out of its context when it referred to one sensory sphere only (sight). When two sensory spheres were involved (sight and touch), his span was passed. He was able to analyze details only without regard to the characteristic "point."

3. *Coincident Analytic and Synthetic Apperception.*—(*a*) Opposites: Thirty adjectives were given with the direction to find the corresponding opposite, e.g., to "quick," "wealthy," "beautiful," the opposites "slow," "poor," "ugly" were to be found. Seventeen opposites were found; thirteen were missed. Of thirty nouns, the opposite was found for twelve and missed for eighteen. The adverbs, prepositions and verbs were almost completely missed.

Sentences were then offered with the order to supplement the omitted opposite. The sentences ran as follows: "Men are either rich or ——"; "men either live or ——"; "men either buy or ——"; "things are either above or ——"; etc. The performance was generally good.

(*b*) Differences and Similarities Between Two Objects or Categories: To pen and pencil he said: You write with a pencil and suck ink with a pen. Door and

window: They are made of glass or of wood. Spinach and meat: Spinach is vegetable, and meat is food. Bread and milk: Bread is food, and milk is a liquid. Ink and water: You write with ink, and water is to drink. Couch and bed: Couch is in the sitting room, and bed is in the bed room. Church and school: I go to school for speech, and they pray in church. Street car and automobile: Street car is on track, and automobile is fed by gas. River and lake: Chicago river flows to a certain point, and a lake is a large body of water, about 250 miles long. Poverty and economy: Poor people have poverty, and economy is saving. Accident and calamity: Accident is a person injured, and calamity is Ohio prison fire. Industry and agriculture: Industry is a business, and agriculture is farming.

Not in one of the pairs was the patient able to indicate properly the points of similarities.

(*c*) Differences in Alternative Situations: The patient was told: Somebody does a lot for his mother, and somebody else doesn't do anything. He said: The one shows gratitude, the other ingratitude.

He was then told: Two boys are attacked by a dog. The one stands still, the other runs away. He said: The one is a coward, the other is not afraid.

He was then told: Two men go into business. The one makes money, the other loses out. He said: The one is a failure, the other is successful.

Comment.—If I say two persons differ in their weight I have established one feature which they have in common (weight) and another feature in which they differ (degree of weight). In establishing the common feature, I synthesize; in establishing the differential feature, I analyze. The statement, therefore, contains both a synthetic and an analytic element. This coincident synthesis and analysis seemed far to exceed the patient's span. He proved defective in all categories. But the relatively best performance was furnished in the adjectives. The reason for this facilitation, offered by the adjectives, seems obvious.

An adjective like "lean" can only be brought under the category of weight, as expressed in pounds. Its opposite is then easily found in the same category. It must be "stout" or "fat" and cannot be "tall" or "quick," as these terms refer to categories of height and movement and not to the category of weight. Adjectives are thus, as a rule, unequivocal, while all the other parts of speech are more or less ambiguous in their categorial affiliation. A noun like "friend," brought under the category "business," means a partner; under the category "family" it means a cousin or brother; under the category "politics" it may mean a partisan, adherent, leader, etc. The corresponding opposites may be competitors, strangers, political opponents, etc. It is similar with verbs. "To begin" can be brought under the category "total act." Its opposite is, then, "to end." But if brought under the category "continuous acting," its opposite may be "to continue" or "to cease" or "to interrupt." Prepositions show the same categorial indefiniteness. "Below the bridge" may be opposed to "above the bridge" but also to "on the bridge," "beside the bridge," etc.

In the sentence series "a man is either rich or ————" the nature of the opposites was pointedly accentuated by the linguistic formula of opposition (either—or) and the task thus facilitated.

Of special interest was the performance of differentiating between two objects (pen and pencil) or two categories (accident and calamity). What was expected was the characteristic difference. A correct answer would have been: The pen needs ink, the pencil does not. Then the two objects would be compared under the common category of "needing ink." A correct answer would also be: Pencil writing can be easily erased, ink script not so easily. The common category would be "durability of the product." In either case, it was again a question of finding the common category (synthesis) and then splitting it into its components (analysis).

This coincident act of synthesis and analysis was outside the patient's span. He failed to find precise, i. e., comparable, categories. When he said: you write with a pencil and suck ink with a pen, he apperceived pen under the category of "needing ink" and pencil under the much wider category of "writing in general." Or he put spinach under the narrow category "vegetable" and meat under the much wider category "food." Such categories do not lend themselves to apperceptive comparison. Only the pairs door and window, couch and bed, church and school were apperceived under mutually comparable, though clumsy, categories.

In the pair series "poverty and economy," "accident and calamity," "industry and agriculture," the performance was distinctly better than in the preceding series. But here the choice of categories was relatively restricted. Poverty and economy could hardly be compared in anything but money. Here the synthesis was already given by the task, and what the patient had to supply was not a coincident act of synthesis and analysis but analysis only.

The performance was still more facilitated in the task of finding the difference between the person who does a lot for his mother and the other who does not. Here the common category was not only implied but mentioned explicitly. The two were brought under the common category of "doing something for their mother."

The failure to bring out the similarities in two objects or two categories calls for a special explanation. It would appear that to indicate the features that are common, e. g., to a pen and a pencil, involves a process of isolated synthesis which ought to be within the patient's span. But, as a matter of fact, this task requires a rather complex act of analysis. Before the common features of two objects can be visualized, all their properties must be scanned and weighed and from the surveyed properties only those selected in which both objects agree. In other words, the process is one of painstaking analysis, followed by a con-

cluding synthesis. What at first sight appears as an act of isolated synthesis, presents itself, on closer investigation, as a complex process of coincident analysis and synthesis.

4. *Additional Tests for Apperception.*—(*a*) Genus and Species: The patient was told: A dog belongs to animals. What does a fly belong to? Answer: Insects. Then he classified in the following manner: horse—animal; violet—plant—flower; orchids—flower; lion—animal; purple—color; brown—color; brass—metal; etc.

(What kind of vegetables do you know?) Apples—turnips—pumpkins—lettuce—

(What kind of trees do you know?) Cherry tree—pineapple tree—apple tree—cherry tree—plum tree—

(What kind of religions do you know?) Catholic, Protestant, Jewish; Chinese worship Le Joshans; the English Church is Episcopalian; the Catholics are German—not all of them—Luther split the church, and they went with him—not all of them—Russian church—no Russian church now—the Soviet took charge of it—the Hungarian church—it's all catholic—Spaniards are catholic, Italy is—France is protestant—but they don't believe in God.

(Which political parties do you know?) Republican, Democrat and Socialist—what is that name of that other party?—popular—populists.

(*b*) Synonyms: He was asked to tell another name for: watch-dial, time piece; doctor—physician; merchant— ————; automobile—autoist— ————; violin— ————; city—Chicago; stool—what you sit on; boots—rubber; trousers — ————.

He was then asked to tell slang words for: alcohol— ————whisky— ———— moonshine, gin; a small child — ————; intoxicated— ———— drunk; policeman — ————cop; father — ————; cigaret — ————pill.

He was told: If I whip a horse, this is called cruelty. How would you call it,

If I give a poor man money? This is———begging———pauper.

If a rich man gives money to a university?—philanthropy.

If a man dies for his country?—hero.

If a man saves a child from drowning?—hero— ————life saver.

If a man spends money recklessly?—spendthrift— ————a fool.

If he does not like to spend his money?—miser.

(*c*) Absurdities: The first four absurdities were taken from the Binet-Simon series (Terman[27]): A railroad accident happened yesterday. It was nothing serious. Forty-eight people died. His answer was: It was a big accident. It's wrong.

A man wanted to commit suicide. But he was afraid to do it on a Friday because Friday is an unlucky day. He laughed and said: It's a dead man.

A boy was found cut in eighteen pieces. The police think he committed suicide. He laughed and said: That's impossible.

What would a man do before starting on an important business? He said: I'd wash up.

A steamboat is 300 feet long, 70 feet wide, 80 feet high. How old is the captain? He laughed and said: That isn't correct.

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27. Terman, L. M.: The Measurement of Intelligence, Boston, Houghton Mifflin Company, 1916.

He was told: I'll ask your advice; I bought a bookcase. Should I place it in the kitchen or in the bathroom? He said: Neither. It goes in the sitting room.

All I have left is a dollar. Should I now buy a ticket for a show or a dinner? He said: Well, the dinner would be favorable. Don't spend the last dollar for a show.

I ask a man what is the time. He said, I don't know, I am a stranger here. He laughed and said: He got mixed up; he should say: one o'clock, two o'clock.

My brother is 12 years old. Next year she will go to high school. He said: It's not correct. A brother and a she are not the same.

I like John although he is a fine fellow. He said: That's correct.

I trust my neighbor because he is dishonest. He said: You couldn't trust a dishonest man.

Comment.—When the patient said, a horse is an animal, he classified the particular category "horse" (species) under the general category "animal" (genus). Similarly, when he said: a man who dies for his country is a hero, he again synthesized "this man" under the general category "hero." Both instances constituted an act of isolated synthesis. They were well within his span. But when he was directed to decompose the general categories "vegetables," "trees," etc., into their subcategories, he had to perform an isolated act of analysis and failed. In analyzing the various religions, he showed some proficiency. But then he rambled off into relatively incoherent and irrelevant details and showed that description, i. e., analysis, taxed his span even in matters which were otherwise known to him.

When instructed to give another name or a slang name for some category, he was expected to classify two coordinated categories side by side without subordinating them under a common broader category. This modified act of analysis again exceeded his span.

When he was told about the railroad accident, he was offered the category "serious fatality," linked to the category "nothing serious." He immediately noticed that such contradictory categories could not be united under a common broader category. In other words, he showed a considerable sensitiveness to faulty synthesization. His responses to the questions for advice were another evidence of this categorial sensitiveness. He instantly realized that the category "bookcase" could not be synthesized with the category "kitchen" or "bathroom."

MEMORY

He was told to repeat: John, Max, Mike, Philip. He said: John, Max, Philip, John and added: It wasn't that way. After one minute he repeated: John ———. After five minutes he said: Mike——that's all.

He was able to repeat after one minute's lapse: Jolly people enjoy happy faces. After two minutes he said: Good friends enjoy happy faces.

From a group of fifteen faces, representing stage stars, three were exposed to view for ten seconds. The three were then mixed with four other pictures. He

picked the first three pictures promptly from among the seven. He was then shown two more pictures and asked to pick all five from among the total of fifteen pictures. This he did promptly.

Comment.—His memory span was quickly exceeded with relatively senseless material (disconnected names). With sense material (connected sentences, pictures) his span was considerably lengthened. Material offered by the visual route was handled with greater ease than auditory presentations.

INTERPRETATION OF PICTURES

The patient was shown, on different days, various pictures, outlines and silhouettes and asked to describe what he saw.

He was first shown the picture of a bust of a man, cut in six equal pieces, and asked to put the pieces together. He did so promptly.

He was then shown nine different parts of dismembered pictures, for instance, the hair, forehead and upper lid of a woman's face, the cut off leg of a man in sitting posture. He interpreted correctly the meaning of the pictures.

He was given silhouettes in black and white of a jockey, a polo player, a golf player, etc., and he designated them promptly and correctly.

He was offered the pictures of a medieval king, a scribe, a Quaker and a man in overalls. The pictures were held in bare outline and were merely suggested by a few scant strokes. He named them correctly.

He was then tested on elaborate pictures, all in all twenty-three. Sixteen of the pictures he interpreted in a single synthetic sentence; seven were described in detail, i.e., analytically.

The following is a typical instance of synthetic interpretation: The picture showed three dogs jumping over a fence. He said: Three dogs, chasing something.

The following is a typical instance of analytic description: The picture represented a library room, with wall pictures, globes and two chairs. He said: Well, I see five pictures and four globes and a bookcase and two chairs——that's about all. I asked him: What is the whole thing? He said: It's a picture of bookcase——two chairs.

Comment.—Of twenty-three elaborate pictures, the patient described sixteen synthetically and seven analytically. He was able to synthesize six parts of a picture into the whole picture. When shown parts of dismembered pictures he supplemented synthetically the whole picture. Silhouettes and crude outlines of men and scenes he interpreted with great facility. On the whole, he showed a considerable skill in synthesizing parts into their whole, in supplementing the whole from isolated parts and in rendering synthetically the meaning of most elaborate presentations.

COMMENT

After seventy years of intense investigation by the ablest workers, the aphasias may be said to represent the best studied and least understood subject in the field of neuropsychiatry. Localization and classification are today, after Marie's and Head's attacks, more tangled than

ever. And as far as the clinical side of the issue is concerned, there seems to be general disagreement as to the meaning of the most fundamental terms. The main controversial points may be summarized as follows: (1) Is agrammatism a really existing clinical entity? (2) Are the aphasias disturbances of both speech and intelligence or of speech alone? (3) Are there many varieties of aphasias, or can they all be reduced to one type? The present discussion will ignore the problems of localization and classification and confine itself to a review of the last three questions only.

What, in the present case, appeared as "agrammatism" was limited only to reading aloud. It is, of course, possible that in the beginning both spontaneous speech and reading aloud were "agrammatical" and that the latter was the residue of an originally more extended lesion. Such residual stages are well known in the course of an "aphasia in restitution" (Bonhoeffer [28]). Be this as it may, the tests showed conclusively that the "agrammatism" had no reference to any inability of handling grammar as such. What appeared, on superficial examination, as a mismanagement of singular and plural, as a confusion of the tenses or of the active and passive voice, was reduced, by means of suitable tests, to the inability of dealing with affixes and particles. But that the mistakes, made in these speech elements, had their root in the intellectual factor of meaning, and not in the linguistic factor of grammar, was clearly demonstrated.

Aphasias with a difficulty of handling the "small" parts of speech have been variously described. In the French literature they go by the name of "style télégraphique." Its opposite is the "style nègre" in which the "small" parts of speech are preserved and nouns, adjectives and verbs more or less lost. The corresponding German terms are "Agrammatismus" and "Paragrammatismus," respectively. The condition found in my patient is identical with the telegram style of the French or with the agrammatism of the Germans.

While no generalizing inference can be drawn from one case, it may be submitted as tentative possibilities: (1) that some patients encounter particular difficulties in manipulating the so-called small elements of speech that have no "meaning"; (2) that the grammatical complexity of such languages as German is primarily due to their superabundance of articles and endings particularly; (3) that patients oriented on "meaning" will of necessity find more opportunities for seemingly grammatical offenses in a complex language, like German, than in a simplified language, like English. A final verdict on this question must be left to future investigations.

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28. Bonhoeffer, K.: Zur Kenntnis der Rueckbildung motorischer Aphasien, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **10**:203, 1902.

Since Broca's [29] classic description, the aphasias have generally been defined as a disturbance of speech with preservation of intelligence. Marie [28] challenged this conception and postulated that Wernicke's zone, the only speech zone within his scheme, is an "intellectual center." A lesion of this center, he concluded, gives rise to a disturbance of intelligence. Somewhat obscurely, he distinguished between a "brutal" intellectual deficit of the dementias and a "specialized" intellectual deficit of the aphasias. Dejerine,[30] Liepmann,[31] Gutzmann [32] and others have polemized against Marie's "heresy" on various grounds. But the controversy is apt to turn into a verbal affray if no precise definition is offered for the terms "intelligence" and "intellect."

In the present study, the approach to the problems of intelligence was phenomenologic. The intellect was considered a unit which manifests itself in observable and roughly measurable phenomena. It was assumed that, by means of the intellect, objects are (1) identified and recognized under their proper categories, and are (2) thought about under the same categories (Owen,[33] Pillsbury and Meader [34]). In order to perform its functions of recognition and thought, the intellect must make use of apperception. While normal apperception will identify a table under the realistic categories of "furniture," "heirloom," "expensive luxury," "necessary equipment," etc., a pathologic apperception may identify the same table as a cow. The result would be a hallucination or a qualitative intellectual defect. If the table is identified as an object, capable of spontaneously rising and making meaningful pronouncements, it would be placed under the apperceptive category of "magic." Magical and hallucinatory apperceptions are not realistic, and hence are qualitatively different from normal apperceptions. In this study it was shown that the various apperceptive spans of the patient were reduced, but that the types of apperception used were invariably realistic. Apperceptive recognition was quantitatively reduced but qualitatively intact.

If two objects realistically apperceived are brought into mutual relation, they are thought of. If one of the objects is apperceived as a table, the other as a twenty-dollar bill, their mutual relation can be

29. Broca, P.: Remarques sur le siège de la faculté du langage articulé, Bull. Soc. anat. de Paris **36**:330, 1861.

30. Dejerine, M. J.: L'aphasie sensorielle, Presse méd. **40**:437 (July 11) 1906.

31. Liepmann, H.: Ueber die angebliche Worttaubheit der Motorisch-Aphasischen, Neurol. Centralbl. **27**:290 (April 1) 1908.

32. Gutzmann, H.: Ueber Aphasie und Anarthrie, Deutsche med. Wchnschr. **37**:1923 (Oct. 19) 1911.

33. Owen, E. T.: Interrogative Thought and the Means of Its Expression, Tr. Wisconsin Acad. Sc. **14**:353, 1903.

34. Pillsbury, W. B., and Meader, C. L.: The Psychology of Language, New York, D. Appleton & Company, 1928.

established in the thought formula: "This table costs twenty dollars." The thought relation is here realistic. But if a schizophrenic person exclaims: "I was born from this table," he establishes a logically and empirically impossible (filial) relation between the table and himself. His thought relations are unrealistic and animistic; therefore, qualitatively defective. That my patient was well able to discriminate between possible and impossible relations between objects was amply evidenced by the spontaneous critique which he applied to sentences like "street-cars dream," "apples sneeze," etc., and by the promptness with which he rejected absurdities. With a quantitatively reduced span his normal quality of thought was preserved.

It is possible that Marie had this quantitative reduction of the intellectual span in mind when he identified the aphasias with a "specialized" intellectual deficit. But his remark that aphasic patients show a "very marked diminution of their intellectual capacity in general" does not seem to refer to a merely quantitative reduction. Nor is such a conception evident from his illustration of the cook who made a mess of the omelet. This cook behaved as would an idiot. If his case was chosen to illustrate aphasic behavior in general, the characterization pointed to a qualitative intellectual deficit. That the cook was, however, merely apraxic is more than probable. Osnato,[35] confessedly a follower of Marie's teaching, definitely identified the aphasias with a qualitative defect of intelligence. Assuming that the tests employed in this study are reasonably reliable, they contradict Marie's and Osnato's hypotheses.

Things can only be properly identified and thought about if they are adequately remembered and attended to. Memory and attention enter, therefore, as an integral part into every intellectual activity. That the patient had a reduced mnemic span, both for retention and for reproduction, was brought out in many tests. But the disturbance of his attention, being of a less clearcut type, calls for detailed discussion.

For the purpose of recognizing and thinking, attention must alternately be concentrated on and shifted from the objects to be recognized or thought about. If the patient is asked to cancel certain letters of a paragraph, he must concentrate his attention on these letters and may overlook everything else, like the correctness of spelling, the logical coherence, etc. But if he is asked to give an opinion on how a man will behave in a storm on the ocean, he had to deal, not with one element, as in the instance of the letters to be canceled, but with a motley variety of factors. He must consider the intensity of the storm, the solidity or frailty of the boat, the intelligence and emotional stability of the man and the various possibilities of protection and escape. He must

35. Osnato, M.: Aphasia and Associated Speech Problems, New York, Paul B. Hoeber, Inc., 1920.

keep in mind that some people are timid, others adventurous, some fascinated by, others indifferent to, the majesty of nature. In such a complex event, attention must shift or rove from one part of the picture to the other. This shifting or roving of attention is identical with what in German is called "Einstellung" (von Kries,[36] Offner,[37] Marbe,[38] Groos [39]). During the shift of attention the various objects are quickly apperceived. A facility for the shifting of attention is, therefore, conducive to quick apperception.

Many of the reactions of my patient can be explained on the basis of his relative inability to shift his attention. An ordinary person will perform with almost the same ease whether he is required to focus attention on the meaning of the reading material or on the spelling (proof reading). He will also read with approximately identical ease the sense sequence "France builds ships" and the nonsense sequence "Builds ships France." My patient lacked this normal agility in shifting attention. Presented with reading material of any kind, his attention immediately took a specific slant and remained almost immovably on the plane on which it had been shifted. The slant of attention depended largely on the type of order given. If the order was to cancel letters, his span was considerably widened. But when directed to read the same material, his span was immediately restricted. In the same manner, his span increased when a paragraph was arranged vertically and contracted when a horizontal arrangement was offered. It was in line with his rigidity of "Einstellung" that he was unable to shift attention from the intellectual to the emotional aspect of an event. It must be noted that this relative incapacity to shift attention affects merely the quickness of apperceptive recognition, which is a quantitative intellectual element. It has nothing to do with the discrimination between possible and impossible relations, i. e., with the quality of intelligence.

While the results of this study refute Marie's apparent claim that the aphasias are a qualitative defect of intelligence, they seem to confirm his doctrine of the fundamental unity of the aphasic disturbances. Practically the entire material, reproduced by means of the test series, turned around the problem of meaning or its equivalent, apperception.

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36. von Kries, J.: Ueber die Natur gewisser mit den psychischen Vorgaengen verknuepfter Gehirnzustaende, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. **8**:1, 1895.

37. Offner, M.: Das Gedaechtnis, Berlin, Reuther und Reichard, 1911.

38. Marbe, K.: Ueber Persoenlichkeit, Einstellung, Suggestion und Hypnose, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:359, 1925.

39. Groos, K.: Das Seelenleben des Kindes, Berlin, Reuther und Reichard, 1923.

Lange,[40] Messer [41] and Wundt,[42] following in the footsteps of Leibnitz and Herbart, demonstrated the close relationship of apperception with the clarity and distinctness of the thought process and, in consequence, with the clarity and distinctness of meaning. The one difficulty that ran like a red thread through all the performances of the patient uniformly referred to a defective function of his apperceptive faculties. His particular handicap was to apperceive the isolated parts of a whole. This was evident in reading aloud, in which the span of performance was measurably increased when the whole of a simple sentence was offered and not its isolated "nonsense" parts. It was equally evident in silent reading in which the span for simple words and simple sentences was considerably greater than the span for isolated letters. The almost complete failure in noncopied writing can also be explained on the same basis. Writing from dictation and after exposure is, even with normal persons, largely a matter of dealing with parts, a dictated or exposed sentence being written in instalments, and not as a whole. In performing arithmetical operations, the patient showed the same difficulty in apperceiving parts analytically (subtraction and division), while his span for apperceiving wholes synthetically (addition and multiplication) was proportionately lengthened. The tests for memory brought out the same partiality for wholes in preference to parts. Disconnected names met with a reduced mnemic span, connected sentences and pictures increased the span. Finally, the bent for apperceiving wholes was demonstrated in his manner of interpreting pictures. Of twenty-three pictures, sixteen were described synthetically as wholes, and only seven analytically as agglomerations of parts.

Of considerable interest were the results of the tests for repeating, praxia and time and space perception. They could all be traced to a relative inability to apperceive the meaning of prepositional and adverbial relations. Thus, even complex words and sentences were freely repeated, except when terms like "uptown" or "downtown" figured in the performance. Similarly, acting was eupraxic throughout, except when prepositions like "above," "below," etc., were to be apperceived. That the marked defect in space and time perception could be put down to this difficulty of apperceiving adverbial and prepositional concepts was obvious. I do not feel competent to interpret phenomena of time and space, as an adequate interpretation would require special knowledge of philosophy and theoretical physics. But it may be sug-

40. Lange, K.: Apperception (English Translation), Boston, D. C. Heath & Company, 1896.

41. Messer, A.: Die Apperception und ihre Bedeutung, Berlin, Reuther und Reichard, 1914.

42. Wundt, W.: Voelkerpsychologie, Leipzig, Wilhelm Engelmann, 1911, vol. 1.

gested that every expression of spatial and temporal relations involves, among other things, specification and analysis. In order to apperceive the sentence "put your hand on top of the table," the patient must first apperceive the table in its spatial environment as a whole, and then specify those parts of the environment which are above, below or beside the table. If this interpretation is correct, all the defective performances of the patient can be reduced without remainder to a relative difficulty in analyzing parts and to a relative preference for synthesizing wholes.

The method of examination was that of measuring the span of each performance. The only function that was merely estimated and not measured was that of spontaneous speech. The superiority of a quantitative method, even if it is only relatively quantitative, over a merely estimating method needs no discussion. It is obvious that only by means of a graded series of tests is it possible to get a survey of the total extent of a lesion. Without it, testing becomes arbitrary and unmethodical. Many cases described in the literature give the impression that some functions were tested only within the span. If the test is not pushed beyond the span the defect of the particular function is not revealed. It would have been easy to state that my patient had no defect of praxia and of repeating if he had not been tested with sentences that contained particles. Likewise, a superficial examination, always moving within the limits of the span, could easily have classified this patient as an example of a "pure" alexia or as an alexia plus an agraphia. It would be of the utmost importance for the study of the aphasias if a uniform method of graded testing could be adopted. Whether the present method is suitable for all cases I am unable to state. I may, however, mention that it was applied to a few other patients and was found to give satisfactory results.

SUMMARY AND CONCLUSIONS

1. A case has been described in which an "agrammatic" disturbance was traced to a difficulty of apperceiving "meaningless" parts of speech.

2. All the defects of the various functions were reduced to a relative inefficiency to analyze parts out of a whole, on the one hand, and to a relative preference for synthesizing parts into a whole, on the other hand. All the symptoms were thus traced to one unifying lesion.

3. The hypothesis that the aphasias represent generally a qualitative defect of intelligence was shown to be challenged by the present case.

4. A method of testing was applied which measured the span of each function. This method was oriented on both linguistic and psychologic principles.

DISCUSSION

DR. D. M. OLKON: I wish to refer to a series of experiments conducted in a seminar of educational psychology at the University of Chicago, under the guidance of Prof. F. N. Freeman, several years ago. Tests were given to a group of graduate students for their ability to recall "senseless words" by the auditory and visual perception routes. It took forty-five trials by way of auditory perception for them to learn accurately and eighteen trials by way of visual perception. When "sense words" were exposed to visual perception by means of the tachistoscope, in 100 trials, 14 per cent showed omission of the last letter or syllable, and 8 per cent of the first letter or syllable.

In a person with aphasia, it may be difficult to evaluate the exact loss of the visual perception content or the loss in the general learned equipment. The archaic learned speech usually shows less involvement. How much may be due to the loss through a memory defect caused by the insult to the brain and how much may be due to a general visual confusion of the mental type is also at times difficult to establish.

The letters that were dropped by Dr. Low's patient would suggest the "confusion drop in a running pattern" rather than a particular agrammatical type of "drop," not unlike those observed in experimental subjects when observing a new type of word.

Dr. Low's work is interesting in that it shows again that in a person with aphasia the mental processes apparently no longer work as well as before the attack and that there is always something definitely impaired in the brain which has to do with higher mental processes. Whether or not this case is a typical agrammatism is perhaps questionable. The dropping of the "s" in plural words or the "e" at the end or the middle of a word or the omission of consonants, affixes and suffixes may show only a defect in attention or confusion, or better still, that the person never had attained great efficiency in spelling.

DR. A. A. LOW: I did not know of the experiments to which Dr. Olkon referred but it is well known to me that in psychologic experiments the subjects are often tested with nonsensical, meaningless words and they do not make as many mistakes as patients with lesions of the brain. Some mistakes are, of course, made by normal persons, too.

ASYMBOLIA FOR PAIN*

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REPORT OF A CASE

In 1927, we observed a patient with sensory aphasia who would have hurt herself severely if left alone. She pushed everything that came into her hand against her eyes, heedless of the pain she thus inflicted on herself. When we studied this patient more carefully, we found that she did not react to pain or only in an incomplete and local way. There was no real defense action. Sometimes there was a local withdrawal; the facial reaction of the patient was that of slight pain. When exposed to a strong faradic current she showed pain reactions, but not a real defense. She never became angry at the examiner, and even seemed to derive some pleasure from the pain. Sometimes she took a needle and stuck herself deeply with it. The patient perseverated in actions once undertaken. The perseveration and the sensory aphasia almost disappeared, whereas the changed attitude toward pain persisted. The patient also did not appreciate threatening gestures and was insensitive to loud noises and sudden flashes of light.

An autopsy was held and the brain was examined in a Weigert series. There was a small vertical lesion in the anterior part of the left second frontal convolution. Another lesion started in the left capsula externa, and continued to the basis of the gyrus longus insulae. The anterior of Heschl's transverse convolutions also showed a lesion, but the medial parts were more seriously affected. The upper part of the first temporal convolution was also affected. The gross lesion was found in the gyrus supramarginalis, especially in its basal parts, but there were also softenings in the medullary parts of the gyrus angularis.

The clinical symptoms had pointed to a lesion near Wernicke's region. Since there were no symptoms attributable to the gyrus angularis, we stated that there may be a center in the gyrus supramarginalis a lesion of which makes appreciation of pain and danger impossible.

Two other cases seemed to confirm the localization of the symptom in the anterior part of the lower part of the left parietal lobe. In one, two tumors were present, one in the left side of the frontal lobe and the other in the upper part of the left side of the parietal lobe and in the gyrus supramarginalis. In the second case, asymbolia for pain was observed after the removal of a tumor of the left parietal region. It can be considered as proved that a lesion of the parietal lobe is the cause of asymbolia for pain.

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Our cases make it probable that the gyrus supramarginalis is the most important point in this lesion. This localization, however, has not yet been definitely proved, since in our first case a slighter lesion of the gyrus angularis was also present, and in the other cases the tumors did not allow exact localization. It is remarkable that seemingly a lesion of a part of the brain between the centers that regulate the attitude toward language (gyrus temporalis) and those that make it possible to construct properly a picture of one's own body (gyrus angularis and adjoining occipital region) should provoke asymbolia for pain. Pain must in some way be brought into connection with recognition of the postural model of the body in order to be appreciated fully.

In some of our cases there was not only a dulling of the appreciation of pain, but the pain reaction also was insufficient, without being definitely apraxic. Every asymbolia for pain is connected with an incapability of reacting fully toward pain. Asymbolia for pain is in some way a phenomenon akin to apraxia, but it is characteristic that it is apraxia only in this distinctive field of reaction to pain and danger. It is known that the upper parts of the gyrus supramarginalis have an especially close relation to eupraxia.

In most cases the condition is spread over the whole body, and is different from the disturbances of perception of pain in cortical lesions described by Foerster and others. In some cases the sensitivity of the lower part of the body is greater than that of the upper part.

We have observed ten cases up to the present time. That such a common symptom has escaped the attention of examiners for so long is probably due to the erroneous opinion that the symptoms are disturbances in attention; our patients, however, were very much interested in pain. In six of our cases typical sensory aphasia was present. One patient showed difficulty in finding the right words. In two the sensory aphasia was slight and disappeared quickly. In one difficulties with speech were present. In five cases we have seen the asymbolia for pain disappear. The disappearance of the asymbolia for pain parallels the disappearance of the sensory aphasia. Two of the patients said that they could remember that the pain had been inflicted, but that they did not feel it. Slight apraxic disturbances were present in some of the cases. In two of the cases the postural reflexes were strongly increased. The apraxia usually became evident only in actions directed against the patient's own body. Two of our patients showed perseverational tendencies in connection with the asymbolia for pain concerning actions. These were cases in which lesions of the frontal lobe were found at autopsy.

CONCLUSIONS

In our experience we find that all types of lesions may be the cause of the symptom—softening, hemorrhages, tumors, syphilis and fractures of the skull. We have therefore come to the conclusion that a lesion in a particular region of the left parietal lobe makes it impossible to build up a full perception of pain. Asymbolia for pain is not alone an expression of a deficiency; there is also a particular attitude toward pain which lacks the integration into a higher propositional act. It is from this remarkable point of view that the disturbances described here, as investigations by Bender and one of us (P. S.) have shown, resemble closely the reactions in a particular group of catatonic cases; but it seems that in the catatonic cases the lack of the reaction to pain has a closer connection with the individual problems of the patient.

ABSTRACT OF DISCUSSION

Dr. Emanuel D. Friedman, New York: Was there hemiplegia or any tendency to motor weakness? I ask the question because in the literature cases of left hemiplegia in persons whose speech center was in the left hemisphere are described, and yet the patients were not conscious of the hemiplegia until they looked at the hemiplegic limbs. Is there any connection between the asymbolia that Dr. Schilder has described and this peculiar phenomenon?

Dr. Walter Freeman, Washington, D. C.: Was this symptom associated only with left-sided lesions?

Dr. Paul Schilder: I wish to emphasize that in most of our cases no hemiplegia was present. However, most of the patients did not appreciate their speech difficulties. This phenomenon is well known in acute sensory aphasia.

It is worth while to mention that in so-called subcortical word deafness the patients often do not react in a sufficient way to loud noises.

Probably the phenomenon of lack of appreciation of pain and danger (noise) has something to do with the phenomenon of lack of appreciation of one's own defectiveness. This is a complicated psychic function that is damaged by a localized lesion of the brain. Indeed I think that there are some relations with the interesting phenomenon that Dr. Friedman has mentioned, but the phenomena are not identical. I believe that a lesion near the Wernicke center probably means that one does not feel either the outward danger or the defectiveness of one's own body.

HERPES ZOSTER OTICUS

REPORT OF CASES *

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The exhaustive research of Hunt [1] on herpes in the geniculate area and adjoining nerves needs no further elucidation on the anatomic side. He has unquestionably established that such herpes occurs in the distribution of the sensory portion of the seventh nerve, at times alone but often associated with the adjoining and closely related fifth, pneumogastric, glossopharyngeal and upper cervical nerves, as well as with the auditory nerve. As Hunt pointed out, for many years herpetic eruptions have been observed and described in the latter distribution, and also in the auditory canal and parts of the external ear, but previous writers failed to recognize that the sensory portion of the seventh nerve was responsible for any part of this area of disturbance. The second and third cervical nerves and the fifth, ninth and tenth nerves were regarded as the sole sensory supply of the ear, and hence naturally the only herpetic zones in that area. Hunt showed conclusively that what is now recognized as the sensory portion of the seventh nerve, derived from the geniculate ganglion, innervates an area which includes a part of the tympanic membrane, the external auditory canal, the concha, tragus and antitragus, the lobe of the ear, and the anthelix and its fossa, and that this area may be involved alone as well as in conjunction with adjacent

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1. Hunt, J. Ramsay: On Herpetic Inflammation of the Geniculate Ganglion: A New Syndrome and Its Complications, J. Nerv. & Ment. Dis. **34**:73, 1907; Otalgia Considered as an Affection of the Sensory System of the Seventh Cranial Nerve, Arch. Otol. **36**:543, 1907; A Further Contribution to the Herpetic Inflammations of the Geniculate Ganglion, Am. J. M. Sc. **136**:226, 1908; The Sensory System of the Facial Nerve and Its Symptomatology, J. Nerv. & Ment. Dis. **36**:321, 1909; The Symptom-Complex of the Acute Posterior Poliomyelitis of the Geniculate, Auditory, Glossopharyngeal and Pneumogastric Ganglia, Arch. Int. Med. **5**:631 (June) 1910; The Sensory Field of the Facial Nerve: A Further Contribution to the Symptomatology of the Geniculate Ganglion, Brain **38**:418, 1915.

nerves. Therefore, to him is due the credit of establishing and delimiting the herpetic zone of the geniculate ganglion, regarded as the sensory component of the seventh nerve.

In a paper by Key-Aberg,[2] reference is made to a case of herpes oticus published by Gruber in 1887, with swelling of the ear followed by herpetic vesicles and facial paralysis. In 1901, allusion is made to fourteen cases of acute infection of one or several cranial nerves, including always one of the three (fifth, seventh and eighth) reported by Hammerschlag. In 1904, Körner likewise published a report of a case of herpes of the chin, with deafness on the right side, right-sided facial paralysis and vesicles localized chiefly in the outer ear and in the orifice of the auditory meatus. According to Key-Aberg it was at this time that the term herpes zoster oticus was generally adopted, but a sharp delimitation of a herpetic zone to the geniculate distribution was not emphasized before Hunt's critical work. In a later paper, Key-Aberg [3] pointed out that ordinary herpes zoster of the body zone has much in common with the varieties confined to the cranial nerves. He believed that an examination of the spinal fluid gives weight to this assumption which, in general, has not been questioned.[4] There is certainly no adequate reason to think that herpes of the cranial nerves has anything distinctive about it from an etiologic standpoint. Its peculiarities depend naturally on the anatomic distribution of the nerves rather than on any more fundamental difference. The fact that the facial nerve is often involved in its motor part is due to no other reason than its close proximity to the sensory branch. No doubt, herpes of the body zones would show similar motor involvement, were it not for the anatomic separation of the dorsal root ganglia from the motor nerves. There is no justification for the assumption that poliomyelitis and herpes are related from the fact that the facial nerve is so often involved in herpes of the geniculate zone. It does not conduce to clarity to speak of herpes zoster in general as a posterior poliomyelitis. Such a clinical designation, apart from causative factors, must lead to confusion in the nomenclature.

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2. Key-Aberg, H.: Herpes Zoster Oticus: Polyneuritis Meatus Audit. Intern. Herpetica, Acta oto-laryng. **10**:209, 1926.

3. Key-Aberg, H.: A Contribution to the Pathogenesis of So-Called Polyneuritis Meat. Int. Herpetica vel non-Herpetica, Acta oto-laryng. **12**:372, 1928.

4. Hunt, however, made the following statement: "I would also emphasize the fact that in my study of this subject, I have found no cases with facial, auditory, glossopharyngeal or pneumogastric nerve complications, accompanying an eruption of herpes zoster, except when situated on the cephalic extremity of the body; i. e., herpes facialis, oticus, pharyngis, laryngis, lingualis, and occipitocollaris" (The Symptom-Complex of the Acute Posterior Poliomyelitis of the Geniculate Auditory, Glossopharyngeal and Pneumogastric Ganglia, Arch. Int. Med. **5**:670 [June] 1910.

The following cases are reported briefly to emphasize the importance of Hunt's observations and to indicate that geniculate herpes is not so unusual as is ordinarily supposed, although often complicated by the involvement of other herpetic zones.

REPORT OF CASES

CASE 1.—The patient, aged 36, the mother of one child, one having died in infancy, was examined in consultation with Dr. William H. Robey on Dec. 20, 1929. Beyond the fact that she had had her tonsils removed fifteen years before, there was nothing of significance in the previous history. On December 20, she had a slight sore throat that did not demand medical attention. On December 17, she called a physician because of a feeling of soreness about the left ear, which was much swollen. There was also a palpable gland at the angle of the jaw. The ear-drum was normal, and there was obviously no disturbance of the middle ear. The condition improved somewhat for a time. However, the patient had marked pain in the mastoid region. She stated that the left side of her upper lip felt as if procaine hydrochloride had been injected. She showed slight improvement until December 18, when facial paralysis developed, involving all branches of the nerve, but more particularly the lower ones. She had varied pain—aching, steady, sharp and intermittent—about the ear. At the outset this pain was rather inconstant. For several days before the herpetic eruption appeared, the patient suffered much from vertigo. She felt as if she were going to fall forward, and as if the automobile in which she was riding was going very fast. She had a similar experience when walking. The vertigo disappeared at the end of three or four weeks. She continued to have some tinnitus until Jan. 1, 1930, about two weeks after the onset. The tinnitus was improved by blowing out the eustachian tube, and when examined on March 19 it had entirely disappeared. She continued to have some slight headache, but with this exception she was entirely well. There was no evidence of any herpetic eruption or of scars. Sensation was everywhere normal.

During the physical examination (December 20) no abnormality was found in the reflexes, pupils or the nervous system in general, except for the condition of the ear and the facial nerve. There was a pronounced facial paralysis on the left side with obvious involvement of all branches of the nerve, although the eye could be closed weakly. The pronounced swelling of the ear noted earlier had disappeared, but the auricle was markedly reddened and at various points showed some vesicles of a distinctly herpetic character. The external auditory canal was practically closed through swelling of its walls. Taste was definitely affected on the left side of the tongue.

Course.—When the patient was examined again about a month later, there was decided improvement. The face had practically recovered its normal motility, with slight persistent weakness in the closing of the lids. The lower branches of the facial nerve had practically recovered, but the patient still noticed a small area of reduced sensation over the left side of the upper lip. The vertigo of which she had formerly complained had disappeared. There were no signs of herpes left, excepting a slight scar in the internal meatus. The Rinne test was positive. The sense of taste had returned. She was able to whistle imperfectly.

Comment.—This case is of interest in that the herpetic eruption was sharply localized in the zone attributed by Hunt to the sensory portion

of the seventh nerve, originating in the geniculate ganglion. With the associated facial paralysis the assumption is not justified that other nerves were involved, beyond the fact that the vertigo is presumably to be attributed to disturbance in the vestibular portion of the auditory nerve (ganglion of Scarpa), which obviously has no herpetic zone. The area of slightly disturbed sensation over the upper lip in the fifth nerve distribution is not readily explainable. There were no signs of a herpetic eruption in the distribution of that nerve, nor other indications of its involvement. The case may properly, therefore, be placed in Hunt's group B, herpes oticus with facial palsy. The tinnitus that was noticed for a time was possibly due to swelling and closure of the external auditory canal. The involvement of taste on the left side of the tongue, has frequently been described in these cases. Usually, as in this case, it clears up quickly after the acute phase has passed. This involvement of the chorda tympani throws some light on the course of the taste fibers, and seems on the whole to indicate that they pass through the geniculate ganglion, by way of the nerve of Wrisberg to the pons, rather than through the fifth nerve by way of the gasserian ganglion. On the other hand, Cushing's investigations have shown that in spite of complete extirpation of the gasserian ganglion, taste is unaffected, which is difficult to reconcile with the participation of the fifth nerve in the function of taste. The frequent occurrence of taste disturbance in the syndrome of geniculate herpes must, however, indicate that the chorda tympani has an intimate relation with the sensory component of the seventh nerve apart from its recognized temporary association with it. The pronounced swelling of the ear that occurred in this case, preceding the appearance of herpes and facial paralysis, was described in one of the earliest cases by Gruber.

CASE 2.—O'C., aged 60, married, a laborer, who was examined on April 4, 1920, at the Massachusetts General Hospital, had had mastoiditis on the left side in 1916. On April 4, 1920, he awoke with a burning sensation on the left side of the face and inability to elevate the left eyebrow. Later, the left ear began to discharge. The facial nerve did not respond to faradism. Two days after admission he was unable to sleep on account of facial pain, and four days later the seventh nerve was paralyzed and herpes appeared in the ear. Two weeks later there was still pain, and the paralysis of the seventh nerve was unchanged. There was nothing in the ear to account for the condition.

Comment.—In this case also the herpes was apparently limited to the geniculate zone. It is of interest that the patient had a suppuration of the middle ear to which possibly the later disturbance in the facial distribution, both motor and sensory, may be attributed, unless one considers that herpes is invariably due to a specific virus.

CASE 3.—In McC., aged 10, who was examined on May 17, 1921, at the Massachusetts General Hospital, herpes developed on the left side of the tongue, followed the next day by swelling of the ear which was "covered with blisters," including the canal. The blisters broke and discharged, following which there was paralysis of the left side of the face of a peripheral type, accompanied by slight deafness. A competent otologist stated that no condition of the ear could account for the paralysis or other disturbance.

Comment.—The interest of this case lies in the fact that herpetic vesicles appear on the left side of the tongue, followed on the next day by a typical geniculate involvement. It is fair to assume that the eruption on the tongue was due to a geniculate involvement because of the complete facial paralysis, although the possibility of participation of the lingual branch of the mandibular (fifth) or possibly the glossopharyngeal nerve is not forthwith to be excluded. From such observations as this, Hunt plausibly concluded that sensory rudiments from the nervus intermedius (seventh) accompany the chorda tympani to its final distribution in the anterior two thirds of the tongue. No note apparently was made of the palatal region.

CASE 4.—C., aged 50, married, who was examined on Dec. 12, 1915, in the Massachusetts General Hospital, had been seized in the night with an earache on the right side, vertigo and nausea. The mastoid was suspected, but excluded. The right auditory canal, in its outer portion and throughout the course of the canal, showed herpetic vesicles. Accompanying this was a complete right facial paralysis associated with diminution of hearing, but without tinnitus. There was no cardiovascular-renal pathology, and examination of the central nervous system otherwise gave negative results.

Comment.—Except for a slight diminution of hearing, this case is a further example of a facial geniculate involvement. It is, however, of some interest that the predominant symptoms were earache, vertigo and nausea, indicating the frequent association of the auditory mechanism.

CASE 5.—S., aged 61, married, a plumber, who was examined on July 26, 1929, at the Massachusetts General Hospital, for the preceding five days had noticed an eruption on the face, neck and upper part of the chest to the midline and to the border of the shoulder, also behind the left ear and in the ear. Two days later he became very dizzy and began to fall forward, and a complete paralysis of the seventh nerve developed. He was confined to bed. When able to get up he had a staggering gait and headache, and the left ear felt as if the auditory canal was full. For a time he had a sensation of numbness in both hands. There was no other disorder of sensation, and there was no paralysis other than that of the facial nerve on the left. The pupils were equal and reacted rather sluggishly to light. The fundus was normal; lateral nystagmus was noted, more marked on fixation to the left than to the right. Paralysis of the left seventh nerve was complete, with tinnitus on the left and deafness. The Eye and Ear Infirmary reported that the condition of the ear was not the cause of the facial paralysis. The facial nerve did not respond to faradic currents.

On Jan. 7, 1930, about six months after the first examination, he stated that he had suffered extremely from tinnitus, deafness, facial paralysis and unsteadiness in gait. The vertigo had on the whole been worse. A detailed neurologic examination otherwise gave negative results.

On January 22, the patient reported that the dizziness was slighty less, and that there had been some improvement in the muscles of the face, but that he was not yet able completely to close the left eye. The ear had not so much the sensation of being plugged. The skin of the face and behind the ear was less numb.

On March 26, there was a persistence of the vertigo when the patient was in an upright position. He was very unsteady in gait; when lying or sitting the vertigo disappeared. He had some persistent pain both behind and in the ear. He was still deaf on the left side. The facial paralysis had not yet fully recovered; there was some secondary contracture in the lower branches of the nerve and movements were limited. The eye could be only imperfectly closed; a few scars were still visible, and there was slight "soreness" on pressure about the ear; taste was normal.

Comment.—This case also obviously involved a number of ganglia, especially in connection with the auditory nerve, as indicated by the staggering gait due to an extreme vertigo and a pronounced lateral nystagmus with tinnitus and deafness. The infection was evidently very severe, as shown by the long persistence of symptoms. At the last observation, about eight months after the onset, the patient was still suffering from vertigo and a persistent facial paralysis. Except for its greater severity, this case resembles case 3 and shows clearly a wide involvement of cranial ganglia. In such a case the possibility of encephalitis should be considered. The slowness and, as yet, incompleteness of recovery is worthy of note.

Case 6.—W., a laborer, aged 60, who was examined on Jan. 20, 1921, at the Massachusetts General Hospital, entered the skin clinic because of a vesicular eruption on the back of the neck, extending from the hair line to the shoulder and definitely limited to the right side of the neck. Five days later, he was admitted to the neurologic clinic for facial paralysis of the peripheral type on the right side and herpes of the right side of the face and the right ear, including the external auditory meatus. There was also slight deafness on this side.

A general examination showed the deep reflexes normal; there was no Babinski sign; there was no ankle clonus, paralysis, atrophy or tremor of the extremities. The spinal fluid was clear and contained 130 cells; the Wassermann reaction was negative and the total protein was 65.5, with an initial spinal fluid pressure of 130 diminishing normally on withdrawal of fluid. The heart was normal. There was a herpetic eruption of the face, neck and ear with many vesicles in the auditory canal. Except for the herpes, the ear was normal.

Comment.—In this case, the herpetic eruption involved the fifth distribution and the upper cervical nerves, together with a geniculate involvement. There was also slight deafness. This case should be included under Hunt's group of herpes occipitocollaris with facial palsy and acoustic symptoms, with geniculate involvement. What significance

should be attached to the spinal fluid observations of 130 cells and an elevated total protein content is not definite, beyond the indication of an infection of some sort. Evidently, in this case a large number of the chain of cranial nerve ganglia were involved, together with the upper cervical nerves.

CASE 7.—A gold refiner, aged 67, who was examined on Dec. 16, 1929, was referred to the Rhode Island Hospital because he had attempted suicide. Two and a half weeks after admission, he complained of a sore throat, particularly on the right side, with pain and difficulty in swallowing; an eruption was noted on the right side of the tongue and the right anterior faucial pillar. The mouth had rather a bad odor. Vincent's angina was suspected. Three days later, facial paralysis developed on the right side, with considerable deafness and pain in the ear, and with herpes in the auditory canal. There were also noticed two vesicles on the right side of the face between the eye and the ear. There was no evidence of organic disease of the nerves apart from this disorder.

Comment.—It is clear that this case comes within the category of the geniculate syndrome, as evidenced by the practically coincident development of herpes in the auditory canal and facial paralysis. In view of the fact that vesicles were observed in the distribution of the fifth nerve, one cannot forthwith say that the herpetic eruption in the cavity of the mouth was due to geniculate involvement. It is possible that this represented an abortive herpes of the fifth rather than of the seventh nerve, in contrast to case 3, in which the herpetic eruption was confined to the geniculate distribution in the ear, lending weight to the supposition that the herpes in the oral cavity was likewise due to involvement of this nerve through the chorda tympani rather than of the fifth or glossopharyngeal nerve.

CASE 8.—C., aged 47, came to the dermatologic clinic of the Massachusetts General Hospital early in March, 1930, stating that three days previously he had had pain and swelling of the inside of the mouth on the left side. The swelling appeared in more or less discrete areas.

On examination at this time, there was no evidence of organic neurologic disorder, except herpes over the left side of the face, extending from the eyebrow to the lower jaw, together with herpetic involvement of the left side of the tongue and cheek. Fourteen days after the appearance of the herpes, he reported at the neurologic clinic with a left peripheral facial paralysis and pain at the back of the neck. He said that a small amount of bloody serum had discharged from the left ear. At this time the herpes had dried up, but there was a definite facial paralysis with some diminution of hearing. Air conduction was greater than bone conduction, but was of shorter duration on the left than on the right. The nerve reacted to faradism. A week later he returned to the clinic; the diminution in hearing had persisted. The active herpetic eruption had disappeared, and the ear drum was normal in appearance. When questioned regarding the bloody serous discharge, he stated that there had been no pain when it occurred on traction of the external ear. At this examination the wall of the external auditory canal was normal in appearance. When last seen, the patient had improved in all respects. It has not been possible to communicate with him since the last visit.

Comment.—In this case it is evident that there were extensive facial herpes and paralysis of the seventh nerve, together with a probable geniculate herpes involving the canal. It seems fair to assume this since there was a bloody serous discharge from the auditory canal with absence of pain on traction of the ear, which is always present with furunculosis of the canal. The herpetic eruption on the left side of the tongue may be explained by the involvement of the fifth nerve. The assumption that it may have been due, in part at least, to the geniculate ganglion is not justified, although of course possible, since the facial paralysis and the herpes of the auditory canal are definite indications of the geniculate syndrome.

COMMENT

Since the publication of Hunt's first paper, a number of cases have been reported by him and others with special reference to the geniculate zone. In 1906, the year of Hunt's first publication, Vail [5] described a case under the title, "Herpes Zoster Auris," in which the eruption was situated on the posterior wall of the auditory canal, near the drum membrane and in the region of the mastoid tip. In this case, described without anatomic detail, no mention is made of accompanying paralysis of the facial nerve or of the nerve represented by the herpes eruption in the ear.

In 1914, Dabney [6] reported a case without facial paralysis. He made no reference to the part played by the geniculate ganglion in the possible production of the herpes observed, and he apparently failed to see the significance of Hunt's work on the anatomic and physiologic side, namely, to demonstrate the existence and delimit the boundaries of the innervation of the sensory root of the facial nerve by means of herpetic eruption.

In the following year, McKenzie [7] described a case with herpes oticus and facial paralysis associated with recurrent laryngeal paralysis. There was also a loss of taste in the distribution of the chorda tympani, with herpes of the tongue and pharynx. In addition there was involvement of the spinal accessory, oculomotor and abducens nerves. The spinal fluid showed thirty-six lymphocytes. Such a widespread implication of motor nerves in the presence of geniculate herpes indicates a deep-seated process, possibly suggestive of encephalitis.

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5. Vail, D. T.: Herpes Zoster Auris, Ann. Otol. Rhin. & Laryng. **15**:434, 1906.

6. Dabney, V.: Herpes Zoster Oticus, New York M. J. **99**:272, 1914.

7. McKenzie: Herpes Zoster Oticus with Recurrent Laryngeal Paralysis, J. Laryng. Rhin. & Otol. **30**:339, 1915.

Emerson [8] reported two cases in 1924, one of which, without facial paralysis, he regarded as due to a streptococcus infection originating in the tonsil. There were 13 cells in the spinal fluid. The second case began with vertigo and pain in the right ear, with accompanying herpes in the auditory canal, facial paralysis and unsteadiness of gait. There were 200 cells in the spinal fluid, 90 per cent lymphocytes. The patient whose condition he thought strongly suggested encephalitis made a complete recovery in from four to six weeks.

Sears,[9] in 1927, under the caption, "Herpes Zoster Oticus," described three cases, one in which there was facial paralysis and another with involvement of the fifth to the tenth nerve, inclusive.

Ginsburg [10] has given an excellent résumé of the subject with the report of a case in which the condition was complicated by herpes of the inferior maxillary nerve and of the oral mucous membrane with pain in the tongue.

Lemaitre, Badouin and Sailly [11] recently reported a typical case of the geniculate syndrome accompanied by frequent auditory involvement. It was remarkable in this instance that there was pain for eight days previous to the onset of other disturbances. The facial palsy developed five days before the eruption, and before the herpes appeared there was pronounced adenopathy in the region of the mastoid (case 1). This long prodromal period with evidence of infection is unusual. Sicard, in discussing this case, remarked that when such pain occurs the facial paralysis is usually severe with pronounced reaction of degeneration.

Louis Raymond,[12] on the basis of a case report, discussed the method of spread to the internal ear and suggested the possibility of a meningeal invasion. He gave due credit to Hunt as a pioneer in the general subject.

Facial paralysis (so-called Bell's palsy) is an extremely common condition, and except in very rare instances it is unaccompanied by a herpetic eruption. When herpes occurs with a motor paralysis it is evident that the etiology of the paralysis must be sought primarily in the conditions that bring about or accompany the herpes. This must occur in the geniculate ganglion which, in a constricted space, lies in the closest relationship with the motor portion of the facial nerve.

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8. Emerson, F. P.: Report of Two Cases of Herpes Zoster Oticus with Special Reference to Their Etiology, Laryngoscope **34**:137, 1924.

9. Sears, W. H.: Herpes Zoster Oticus, Ann. Otol. Rhin. & Laryn. **36**:361, 1927.

10. Ginsburg, L.: Herpes Zoster Oticus, Ohio State M. J. **24**:624, 1928.

11. Iemaitre; Badouin, and Sailly: Zona de l'oreille avec paralysie faciale-adénite zosterienne pré-éruptive, Bull. et mém. Soc. méd. d. hôp. de Paris **51**:503, 1927.

12. Raymond, Louis: Paralysie faciale zosterienne, Presse méd. **36**:507, 1928.

The paralysis is therefore doubtless brought about by the pressure of the inflamed and swollen ganglion, and must therefore be regarded as a purely secondary and by no means necessary accompaniment of the herpes. Cases have been reported, for example, those of Dabney, Emerson and Hunt, in which with pronounced herpes there was no coincident involvement of the motor branch. Presumably, therefore, the coincident facial paralysis is merely an expression of the greater severity of the ganglionic infection, excluding the unlikely possibility of coincidence.

Herpes of the geniculate ganglion may lead to certain diagnostic difficulties to one inexperienced in oral diagnosis, as suggested in the case reports. Mastoid disease and possibly labyrinthine suppuration may be suspected. A competent examination at the hands of a skilled aurist should avoid this pitfall. Pain, often of neuralgic type, should not forthwith be attributed to the fifth nerve, as has often been done in the past. In general, more attention is being paid to the sensory cranial nerve ganglia other than the gasserian in the causation of pain about the face, as, for example, in the course of the glossopharyngeal nerve or in severe otalgia. As Hunt again pointed out, the sensory branch of the seventh nerve probably plays a much more important part in these disturbances than is ordinarily recognized quite apart from a herpetic eruption. It is not surprising that the nomenclature of herpes zoster oticus of the cranial nerves has become somewhat involved. Various terms have been used to describe the type in which the ear plays a definite part, but no really satisfactory inclusive term has been generally used. The special emphasis that Hunt placed on the part played by the geniculate ganglion and the fact that he demonstrated that herpes of the sensory portion of the seventh nerve may occur independently of other involvements justifies the term geniculate herpes or geniculate syndrome for the designation of this particular variety. The frequent complications, however, of other nerves, as described by all writers on the subject and again illustrated by our cases, necessitates a broader term, which herpes zoster oticus covers in part. One must, in general, have recourse to a statement of the nerves involved in any individual case, and if the terminology aspires to accuracy, Hunt's classification and terminology can hardly be improved. We can see no justification for the use of the term posterior poliomyelitis to describe any of the cases of herpes.

Especially important is the evidence that Hunt has given to show that rudiments, at least, of the sensory seventh nerve sufficient to be the seat of an occasional eruption limited to the anterior two thirds of the tongue as well as to parts of the palate persist in man. That the slight degrees of sensory disturbance are dependent on the rudimentary

character of the sensory field of the geniculate is to be expected not only from its inconspicuous size, but on account of interlacement with other nerves.

The significance of Hunt's work lies primarily in the fact that he demonstrated the sensory component of the seventh nerve by the ingenious method of studying its herpetic zone, not only in the ear, but also in the oral cavity. This "herpes zoster method," as he called it, has thrown definite light on the distribution of this little recognized nerve and has established relationships which from the anatomic side alone are difficult, if not impossible, of demonstration.

SUMMARY AND CONCLUSION

Our object in this communication is to draw attention again to the importance of the often unrecognized syndrome of geniculate herpes. Eight cases are reported illustrating herpes practically limited to the geniculate zone and others involving adjacent nerve distributions. It should be emphasized that geniculate herpes is by no means rare; that it should be suspected in otalgia and pain generally about the ear; that it usually, but not invariably, is associated with facial paralysis, and that it is often combined with herpes of adjoining nerves.

Abstracts from Current Literature

ON THE DOUBLE INNERVATION OF THE INTERNAL RECTUS MUSCLE OF THE EYE. M. MARQUEZ, Rev. d'oto-neuro-opht. **8**:343 (May) 1930.

The fact that the internal rectus muscle of the eye is associated at times with the internal rectus of the opposite side (in convergence) and at other times with the external rectus muscle of the opposite side (in looking to the side) has been the subject of a series of anatomic, physiologic and chemical investigations which have tried to explain it, without complete success up to the present time. This question is discussed in an effort to clarify it more, basing the conclusions on observed clinical facts and on the knowledge actually possessed of the fine anatomy of the nervous system. Clinical cases from the author's experience, as well as from others, are cited, in order to draw deductions from them in analyzing the schemas already proposed, followed by a description of his own schema.

Parinaud had already noted what Cantonet later called "paralyses of functions" of certain muscles associated with certain others, with persistence of the integrity of the same function when they act synergically with still other muscles. One was obliged to admit the independence of these functions which Sauvineau and later Parinaud explained by supposing the existence of supranuclear centers and of connections between the various nuclei, which enables one to comprehend why certain functions persist unaltered while others are abolished.

A case frequently seen clinically is one in which there is insufficiency of the internal rectus in its association with the homonymous muscle of the opposite side, especially visible in the fixation of the finger of the observer at a certain distance and, if one requires, a sustained convergence of the subject. Then, at the end of a certain time, one or both eyes diverge suddenly. It is thus beyond doubt, in this case, that it is not the function of the muscle itself which is affected but the nervous impulse capable of determining a contraction when it follows a certain pathway is incapable of doing so when it follows another. It is, then, the innervation that is insufficient. In other cases the reverse is observed: the internal rectus cannot follow the external rectus of the opposite side in turning the eyes laterally while convergence remains perfectly normal.

Descriptions of several cases of various ocular paralyses from the literature and the author's observation are given in the following paragraphs.

A personal observation which was a typical case of alternate inferior pontile paralysis, Millard-Gubler type, is mentioned. Autopsy showed a focus of softening in the left side of the inferior part of the pons. The patient had presented a paralysis of the facial and of the external motor oculi on the same side as the lesion and of the limbs on the other side. The lesion involved, especially, the ventral portion of the pons and did not cause any associated ocular deviation—negative data of great value.

In the discussion of the various schemas, only ocular movements due to visual excitations were considered.

These movements of the eyes are of two kinds: (1) those in which the optic axes are parallel and are directed always in the same direction, movements of direction, and (2) those in which the visual axes are directed in two opposite directions, having the tendency to approach each other or to be separated, movements of distance.

Movements of direction can be made in all directions, on the horizontal plane, on the vertical plane or on an oblique plane. Those of distance are possible only in the sense of convergence or of divergence of the ocular axes. This study will be limited to movements of distance and of direction made on the horizontal plane.

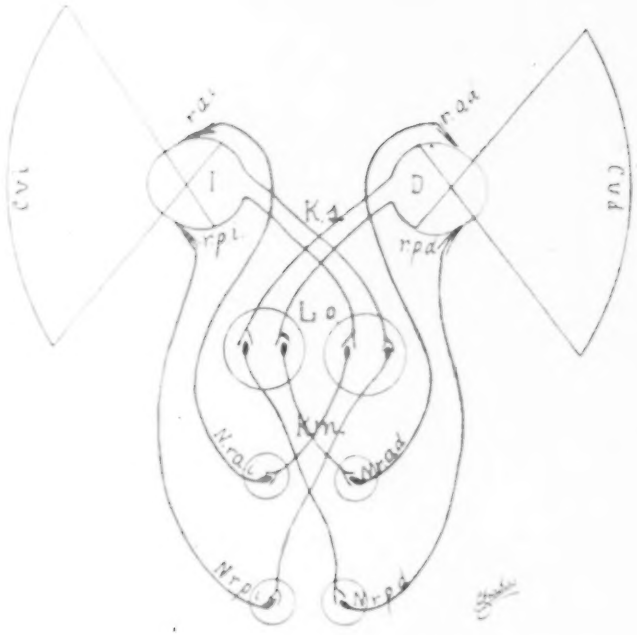

Fig. 1 (fig. 18, Marquez).—Sensory chiasm, *Ks*, and motor, *Km*, completely crossed in animals with independent visual fields (panoramic vision of Cajal). *L.o.* indicates optic lobules; *N.r.a.d.* and *N.r.a.i.*, nuclei of the anterior (internal) recti, right and left; *N.r.p.d.* and *N.r.p.i.*, nuclei of the posterior (external) recti, right and left; *C.v.i.* and *C.v.d.*, left and right visual fields.

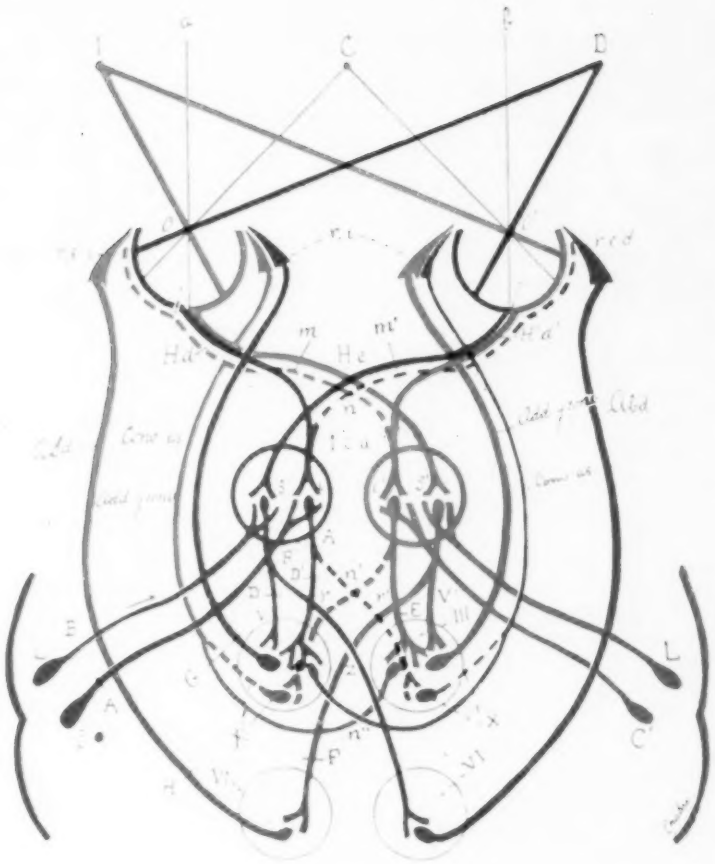

Fig. 2 (fig. 19, Marquez).—Schema of the muscular associations in lateral gaze and in convergence (Marquez). (Green: that which concerns vision and gaze to the left, *I*; red: toward the right, *D*). *Hc* indicates crossed bundle of the sensory chiasm; *H.d.* and *H'.d'*, direct bundles; interrupted line, *m*, *m'*: fibers crossed at *n*, which have disappeared in higher animals (compare with fig. 1); *T.c.a.*, anterior quadrigeminal bodies or primary optomotor centers; *S*, *S'*, neuronal articulations between the crossed bundles and the crossed mesencephalic neurons; crossed fibers at *z*, destined to the nucleus of the external rectus; *V*, *V'*, direct fibers of these neurons; *i*, *i'*, neuronal articulations between the direct bundles of the sensory chiasm and the direct neurons, *r*, *r'*, of the motor chiasm; *n'*, decussation of the neurons which have disappeared (?) in the higher animals; *X*, *X'* direct (?) radicular neurons of the nucleus of the third pair, corresponding to the internal rectus. Has the anterior arrangement been replaced by the direct neurons, *r*, *r'*, and by the decussation, *n''*, of radicular fibers of the third pair? Do both arrangements exist? *III*, nucleus of the internal rectus of the third pair with direct radicular fibers for convergence and adduction associated with the opposite external rectus and crossed for convergence associated with the opposite internal rectus; *VI*, nucleus of the external rectus; *L*, cortical center for gaze to the opposite side; C, the same for convergence; A, B, lesions seated in the central nuron; *A'*, *B'*, the same in the mesencephalic neuron; *D*, *D'*, the same in the direct pathways of adduction associated with abduction of the opposite side and of convergence associated with that of the opposite side, respectively (see text). The double innervation of the internal rectus may be seen, while that of the external rectus proceeds from the centers of the opposite side, that of the internal rectus in adduction and in convergence proceeds from the hemisphere of the same side and, par contra, that of associated convergence proceeds from the opposite side.

Several schemas already proposed, the data of which are chiefly found in the work of Lutz and of Graux, are reviewed.

It is indubitable, according to physiology and pathology, that there exist in each cerebral hemisphere centers of direction of the gaze toward the opposite side (apart from those of the ascending and descending gaze which we will leave aside). Grasset and Landouzy, almost simultaneously in 1879, established their well known law: in lesions of the hemisphere, the eyes look toward the limb in convulsion, that is, to the side opposite the lesion, or if away from the limb in convulsion, then toward the lesion, if it is mesencephalic. Thus each hemisphere controls the external rectus of the opposite side and the internal rectus of the same side, the decussation being seemingly situated in the mesencephalon at the upper part of the pons, above the decussation of the fibers for the trunk and limbs, which occurs in the pyramids of the bulb. This arrangement explains the divers types of alternate paralysis: either the well known syndromes of Webb and Millard-Gubler when there is no participation of the oculogyrals (i. e., when the lesion is ventral, seated in the foot), or the divers types of Foville (peduncular-superior, pontile-inferior, pontile) in which the lesion is dorsal, seated in the tegmen. All this, as Grasset remarks, is conformable with the idea of the existence of a sensory and a motor chiasm, a fundamental idea which the Master of Montpellier condenses in this phrase: "We see and we look at with each hemisphere that which lies in the opposite side of space." We see the opposite side thanks to the sensory chiasm; the impressions coming from this opposite side of space arrive at the primary optic centers, and finally, at the brain, following the optic tracts or hemioptic nerves resulting from the union of the fibers coming from the two homologous halves of the two retinas. We look to the opposite side of space thanks to the motor chiasm either by purely reflex reactions and at the level of the primary optico-motor centers (anterior quadrigeminal bodies) or, after the excitation has reached the brain by the primary opticosensorial centers (external geniculate bodies) and has descended as a centrifugal current toward the aforementioned primary optico-motor centers, by intermediate neurons, from the latter to the nuclei of the ocular motor nerves and finally from there, to the muscles carrying the gaze to the opposite side. The hemioculomotor nerves (or oculogyral nerves—right and left gyral of Grasset) are thus perfectly comparable to those which he called hemioptic nerves, as the homonymous hemianopias are comparable to the conjugate deviations of the eyes, almost always coincident with those of the head in the same direction.

Grasset says, "each internal rectus muscle receives, in addition to a branch of the oculogyrus of the same side a branch from the opposite side. The internal recti muscles are thus innervated, each by the two hemispheres and by 2 different nerves, the oculogyral and the convergent." The author is not in agreement with Grasset on the question of the course of the fibers nor on the spot where the center for convergence is located.

The author's schema was inspired by the famous schema of Cajal concerning the chiasm and the nervous decussation already spoken of. Each of the elements that intervene in the visual act is analyzed in order to arrive at the study of the various segments where ocular movements are effectuated: either automatic and reflex or voluntary.

Among the inferior animals with panoramic visual field, in which the sensory chiasm is totally crossed (*Ks*, fig. 1), the motor chiasm (*Km*), existing in the mesencephalic neuron, must by analogy be also totally crossed in order to permit the excitations from one eye to be conducted to the muscle of the same eye, supposing always that fibers from the mesencephalon are direct.

"Since the images are delineated in the eyeground at a point of the retina opposite to that of the object, and since the anterior and posterior poles of the eye move in an inverse sense, it is necessary, in order to carry the fovea centralis in the direction of the object, that there be contraction of a muscle or muscles, capable of moving the anterior pole in a direction opposite to that of the retina affected. It proceeds from this that the excitation of the anterior part of the retina (internal in higher animals) produces contraction of the posterior (external)

rectus muscle and that of the posterior (external) part provokes contraction of the anterior (internal) rectus. Among these animals binocular vision does not yet exist and thus each eye can be moved independently, which is not the case in animals with binocular vision where it is always a matter of associated movements.

"1. For the ocular reflex movements, we envisage the pathways of relation: (1) between the sensory pathway and the anterior quadrigeminal body (first visual and extraretinal neuron), (2) between the quadrigeminal bodies and the ocular motor nuclei (second intermediate or mesencephalic neuron), and (3) between the nuclei and the muscle (peripheral motor neuron).

"2. For automatic and voluntary ocular movements the connections are: (1) in two centripetal neurons which are, the first peripheral visual neuron mentioned, which, instead of going to the anterior quadrigeminal body, goes to the external geniculate body, and the second visual or central neuron which goes from the geniculate body to the cortical center in the calcarine fissure; (2) in the intermediary neurons of association between the cortical center and the center for ocular movements, situated probably on the external face of the parieto-occipital lobule; (3) in the central centrifugal or descending neurons which go from the cortical motor center to the anterior quadrigeminal body; (4 and 5) in the same mesencephalic and peripheral neurons previously cited. This is, at least, what seems to arise from actual anatomic and physiologic knowledge and from clinical and postmortem data.

"Let us compare again the schemas (figs. 1 and 2). In proportion as, in the animal scale, the lateral direction of the visual axes, with visual fields totally independent, progressively disappears in order finally to become anteroposterior with a common visual field, the most external fibers of the sensory chiasm begin to no more decussate and the direct bundle appears. This bundle is still very small in certain animals with small common visual fields, but in the anthropoids and in man this crossed bundle is almost equal to it without being completely so, for there exist in the most external parts of each visual field a small zone belonging exclusively to the eye of the same side, which corresponds in the retinas to the most anterior part of the nasal halves, from where go forth crossed fibers without equivalent in the direct fibers of the temporal halves.

"The ascending optic nerve pathway of the optic tract or hemioptic nerve is divided into a central optic pathway and into a reflex tract; the latter, which is the pathway of the pupillary reflex to light and of the muscles, goes to the anterior quadrigeminal body and there its fibers penetrate and are distributed to the cells of the superficial and deep layers (longitudinal of Cajal) and arborize. From there leave the fibers (transverse of Cajal) which decussate in large part (decussation of Meynert) and constitute the tectobulbar bundle. The excitations reach the motor nuclei by borrowing either this tectobulbar bundle or the posterior longitudinal bundle, or the system of radiated fibers. There exists then an anatomic substratum sufficient to warrant the thought that the intermediate neurons have their origin in the anterior quadrigeminal bodies and that the crossed pathway is more important than the direct (Cajal).

"Let us recall again that among the oculoperipheral motor neurons, those of the sixth pair are wholly direct, those of the fourth pair crossed and those of the third pair in large part direct and in part crossed. For that which concerns the latter we recall also that one does not yet know certainly to which part of the nucleus of the third nerve they belong, although it is probably to that of the small oblique (by analogy with that which is true of the great oblique, i. e., the fourth pair) and to that of the internal rectus, as Monakow, Terrien, Bernheimer and others believe.

"In spite of some contradictory facts, the anterior quadrigeminal bodies seem to be the coordinating (or supranuclear, Sauvineau) centers for ocular movements of visual origin, in agreement with old opinions of Adamück, Beannis, Knoll, Prus, Bechterew, etc. They are then the centers from which the intermediary neurons, which constitute the oculomotor chiasm of Grasset, depart. As we said in 1901,

in our work on the motor decussations of the visual apparatus, we can conceive this chiasm in the following way: 'to the disappearance of the sensory decussation of the external optic fibers of the chiasm (direct bundle) has followed the disappearance of the decussation of the reflex fibers in relation with them, that is to say, those of adduction (V, V') while the fibers for abduction (Z) conserve their primitive decussation. By analogy with the sensory chiasm, there exists a motor chiasm, with the difference that, in the latter, the crossed fibers belong to the external rectus while the direct are destined to the internal rectus.

"To what was said then we can add today that in the transition of the inferior vertebrates with individual visual fields to the superior with a common binocular field (at least, for the most part) the disappearance of the crossed neurons (n, broken lines in fig. 2) has been followed by the disappearance of the corresponding mesencephalic ones (which cross at n'). The latter transmit the nervous impulses to the direct radicular neurons (X and X') of the third pair in relation with the internal recti. We could suppose that these crossed neurons (n') have been replaced by the direct neurons (r and r') and that, for their decussation, has been substituted the crossed radicular neurons (n''). Thus one can explain the associated convergence of the internal rectus, for the neuron r is articulated both with the one of convergence on its side and with that of the side opposite to the movement, issuing from the nucleus under the form of crossed radicular fibers (n''). On the other hand, the nervous impulse, coming from the nasal half of the retinas, reaches, by the crossed bundle of the chiasm, the neuronal articulations S and S', and next, by the crossed pathways Z, the nucleus of the sixth pair of the opposite side; moreover, by the direct branches V and V', it goes to the nucleus of the third pair of the same side. It is then easy to comprehend the association of the internal rectus of one side with the external rectus of the other in the lateral gaze.

"To resume, when a luminous impression strikes the internal half of the retina, the external rectus of the same side contracts at the same time as the internal rectus of the other side. When the temporal half of the retina is excited, a contraction of the internal rectus of the same side is provoked and that induces contraction of the internal rectus of the opposite side. It never happens that, by excitation of the internal rectus of one side, a contraction of the external rectus of the other side is produced, while, as we have just seen, the reverse does occur. So much for the reflex motor optic pathway; let us now study the voluntary pathway.

"We know that the central optic pathway goes from the lateral geniculate body, by the optic radiations of the internal capsule and the oval center, to the visual center in the cortex: calcarine fissure and its surrounding zone. The voluntary optomotor pathway descends from the corresponding cortical center (curved fold, occipital cortex?), perhaps by the external capsule and the peduncular handle (anse), to the anterior quadrigeminal body where it has a synapsis with the intermediate mesencephalic neurons; for the latter are both reflex pathways for ocular movements and intercalated neurons in the descending series in the case of voluntary contraction (of cortical origin). These intercalated neurons must have adapted themselves to the peripheral sensory pathway as well as to the oculomotor cerebral pathways.

"The quadrigeminal bodies and the neurons which originate there have a special significance: while in the inferior animals the optic lobules are at once reflex centers and centers of sensory perception, in the higher animals their importance diminishes considerably as optoreflex centers and they connect with the brain by the descending pathway. In the inferior animals, experimental lesions of them are followed by symptoms of visual disturbance while in the higher animals and in man, destruction of them by pathologic lesions does not produce visual troubles, properly said, if they do not infringe on the adjacent optic centers or pathways; par contra, they produce disturbance of associated movements of gaze, vertical, upward and downward and lateral. Bechterew remarked that excitations of the occipital and temporal cortex are followed by ocular movements if the anterior

quadrigeminal bodies are preserved intact, and the experiments of Prus show that on stimulating a quadrigeminal body in its external part, a lateral deviation of the eyes to the opposite side is produced.

"From all the preceding and thanks to histologic data, which demonstrate that, to the anterior quadrigeminal bodies, come fibers, on the one hand from the sensory optic pathway and on the other from the cortex, it must be admitted that the anterior quadrigeminal bodies correspond to what Sauvineau has described under the name of supranuclear centers; par contra, these latter seem to have no relations with the frontal cortical sensitivomotor center. The anterior quadrigeminal bodies can then be considered a crossroads where converge: the centripetal fibers of the optic pathway, the corticofugal fibers coming from the centers for ocular movements and the descending intermediate neurons to the ocular motor nuclei, constituting the oculomotor chiasm. We consider the latter as being formed by crossed fibers going to the nucleus of the sixth pair and of direct fibers going to the nucleus of the internal rectus of the third pair and which have been considered by various authors as doubled and crossed. Moreover, we think that, in the same way as the central optic fibers are direct from the lateral geniculate body to the cortical center, the corticofugal motor fibers are also direct from the cortex to the anterior quadrigeminal body. Thus the decussation for the external rectus does not take place in the central neuron but in the intermediate quadrigeminal-nuclear neuron (*Z*, fig. 2), contrary to the opinion of other writers, in particular Bernheimer, who believe that this decussation takes place in the central neuron.

"We believe that numerous physiologic and pathologic facts can be explained by our schema.

"*Physiologic.*—1. In the lateral gaze, the excitation comes from the point *D* (fig. 2), situated for example on the right, stimulates the nasal half of the retina of the same side and, by the crossed bundle of the chiasm, reaches the anterior quadrigeminal body of the opposite side, and from the latter, by the crossed mesencephalic pathway, reaches the nucleus of the right external rectus and, by association with the direct fibers, goes to the nucleus of the left internal rectus. The excitation from *D* stimulates at the same time the temporal part of the retina of the opposite (left) eye and is transmitted by the direct fasciculus of the chiasm to the nucleus of the internal rectus of the same side; thus the two muscles which turn the eye to the right contract, innervated by the dextro-oculogyrus of Grasset.

"On the other hand, according to what has just been said, excitation of the temporal half sets up, by association, contraction of the opposite internal rectus (by decussation at n' or by radicular decussation at n'').

"To resume, excitation from *D* provokes contraction of the right external rectus, of the left internal rectus and of the right internal rectus; but while the internal rectus of the left eye receives two excitations, the right eye receives two antagonistic excitations: one for contraction of the external rectus and one for contraction of the internal rectus, the first being predominant.

"2. In convergence, the stimulus coming from *C* affects the two temporal sides of the two retinas, and the excitation, transmitted by the direct fibers of the sensory chiasm, reaches each internal rectus by neurons, likewise direct, of the motor chiasm, which causes convergence. Moreover, the stimulus would radiate from one side to the other either by neurons crossed at n' in case they persist as vestiges of the ancestral arrangement of the inferior animals, or by the crossed radicular fibers at n''; the contraction of the two internal recti would thus be reinforced, for each of them would contract from a double motive: (*a*) by stimulus emanating from the temporal part of the retina of the same side and (*b*) by that which comes from the opposite side (a sort of consensual reflex convergence). If we now envisage the orders which come from the cerebral cortex we will note once more that the fibers are direct up to the center for ocular motor coordination and that their decussation takes place in the intermediary neuron; they are next again direct in leaving the nuclei of the third and sixth pairs. We must, moreover, draw attention to the fact that as Monakow, Bernheimer and Terrien show in their schemas crossed radicular fibers in the peripheral neuron for the internal rectus

we also admit the possibility that some of these fibers belong to the internal rectus for the associated movement of convergence. These fibers are represented in our schema by decussation at n''. As Cajal remarked in his work on the chiasm, the crossed pathways are always more important than the direct. Let us study now what happens in the combined movements of convergence and direction. In reality all binocular movements are movements of direction and convergence, for, if in the first the two visual axes are directed parallel in the same direction, one may consider this as a convergence at infinity, while, in the movement of what is

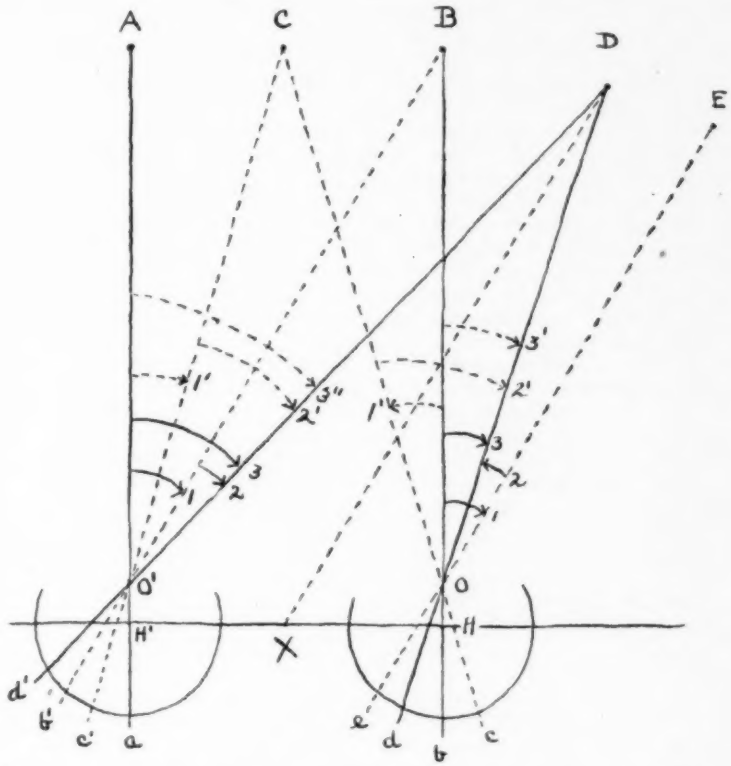

Fig. 3 (fig. 20, Marquez).—Combined movements of direction (in this case to the right) and of convergence (Marquez). aA and bB indicate ocular axes in primary position; $b'B$ and eE, movements of direction to the right (parallel to XD) after having described an angle, *1*; $d'D$ and dD, axes directed to D in a movement of convergence, after having described an angle, *2*, of the same direction as the angle *1* in the left eye and of a sign contrary to that in the right eye. The angle *3* equals *1* plus *2* in the left eye, and equals *1* less *2* in the right eye. Analogous considerations could be made for the angles *1'*, *2'* and *3'* if one supposed first a movement of convergence toward C and afterward a movement of direction toward D. For the left eye *3'* equals *1'* plus *2'*, and for the right eye *3'* equals *2'* less *1'*.

commonly called convergence of distance, the movements are nothing else than movements of direction of the two eyes toward the same point in space.

"In our work, already cited, on decussations we have remarked that all ocular movements, having no other end than to bring the fovea centralis in the direction

of the object (this happening at once in the two eyes), are already movements of convergence. There is no essential difference between the two movements, direction and convergence.

"Let us suppose, for example, that in front of a subject whose gaze is directed horizontally forward (i. e., with the axes parallel and looking at infinity) an object *D* (fig. 3) appears on the right side. The impression will be made in the left eye at *d'* and in the right eye at *d;* as *d* is nearer the fovea than *d'*, contraction of the right external rectus will be less energetic than that of the left internal rectus. In fact, we could suppose that the displacement of the visual lines *A B* into *D* would be in two stages: (1) the two ocular axes pass from *aA* and *bB* to *b'B* and *eE* (parallel to the line *XD* which passes the point *D* and the central point *X* of the base line *HH'*), this being solely a movement of direction to the right without convergence; (2) the two lines *b'B* and *eE* converge on *D* and are placed on *d'D* and *dD*.

"While in the left eye the angies *1* and *2* are of the same direction and their sum is *3*, in the right eye and the angle *1* is made toward the right and the angle *2* toward the left (thus in opposite directions) and their resultant *3* is equal to their difference. It would be the same if we had supposed that the movement of convergence of the visual lines at *C* had been effected first without change of direction and if next the two lines already united at *C* would have been displaced to *D*.

"In the two cases, for the left eye the excursion is the addition of two movements with the same sign, convergence and adduction; for the right eye it is algebraic addition, i. e., the difference between two excursions with contrary signs of abduction and convergence.

"If we consider only the direct distances, it seems that the eye nearer the object appearing in the visual field is the one which makes the smaller excursion, but if we envisage the excursion decomposed into its two terms of addition, direction and convergence, the two eyes verify all together the same angular excursions, which are of the same sign for the eye of the opposite side and of contrary signs for the eye of the same side.

"*Particular Cases.*—1. The point of convergence is found on one of the visual lines (*B*, for example); in the right eye the angles *1* and *2* being then equal and with contrary signs the angle *3* is *0*. That is to say, in this case the visual line of the right eye does not vary because the contractions of the internal rectus and of the external rectus balance each other.

2. The point of convergence is between *B* and *C*: in this case, for the right eye, the angle is $1 < 2$; there is, then, predominance of the contraction of the internal rectus over that of the external rectus.

3. The point of convergence is *C*, exactly in the median line: the angle *3* is given in the two eyes by the contraction of only the corresponding internal rectus. It is then a case of pure convergence, for in the left eye the additive factor (adduction) and in the right eye subtractive (abduction) are nul. In each eye, then, the angle $1 = 1' = 3 = 3'$.

"En resumé, we believe that we have demonstrated by anatomic and physiologic considerations the combination of the two categories, movements of direction and of convergence in the two eyes in binocular vision.

"*Pathologic Facts.*—These also find explanation in all the preceding, and given the importance which we have already accorded them, we will review those which best explain our schemas.

"The laws of Grasset and Landouzy on conjugate deviations, according to whether the lesions are irritative or paralytic, are explained in supposing the lesions are seated either in the cortical centers or in the fibers which leave them to go to the anterior qaudrigeminal bodies, and lesions of the fibers uniting the latter to the motor nuclei.

"Those which involve the cortical neurons (fig. *2B*) of the oculogyres cause abolition of voluntary movements with persistence of reflex movements of visual origin. Interruption of the corresponding neurons of convergence (fig. *2C*) should not totally abolish this function when the lesion is unilateral owing to its

double origin in the two hemispheres. However, on the side of the lesion this function would be more affected. *A priori*, it seems that there should not be total abolition since the influence of the opposite hemisphere persists, if we leave aside the exceptional cases of double lesion.

"Can the mechanism of the production of strabismus be thus explained, agreeing with Parinaud, in admitting the interruption of the pathway of convergence which leaves intact the movements of direction, those of convergence existing in excess or deficit? It is a question still to be elucidated.

"In the case of lesion of the motor chiasm seated in the nuclear quadrigeminal neurons, it must be a question of facts similar to those which were mentioned in our work on the pupillary fibers and the system of Argyll Robertson and there will be different varieties according to the extent of the lesion, according to whether fibers or centers are affected or according to whether they are irritative or paralytic. There will be, then, diverse manifestations either in the function of the oculogyres, in convergence, associated or not with troubles of the cephalogyres, or of the pyramidal tract and the mesencephalic neuclei, given the so restricted zone of the motor chiasm, the delicacy of the fibers and the frequency of their lesions, most often vascular, syphilitic, etc., and their character, irritative or paralytic.

"Here are some examples: Paralysis of associated movements of laterality (or ocular hemiplegia) from a lesion at *B*, for example, for the right oculogyrus: paralysis of the right external rectus and internal rectus in adduction in associated gaze with conservation of the internal rectus in convergence. Lesion at *D*: paralysis of the left internal rectus in associated gaze with the right external rectus, with persistence of its function in convergence. Lesion at *D'*: abolition of contraction of the internal rectus in convergence with persistence of its function when it acts with the external rectus. These last two cases are varieties of anterior internuclear ophthalmoplegia.

"Complete paralysis of the internal rectus of one side: lesion at *G;* that is to say, peripheral paralysis of the internal rectus for convergence and adduction. Lesion at *F:* posterior internuclear ophthalmoplegia; that is to say, of the external rectus, in reality not to be differentiated in its character from a peripheral lesion at *H*.

"The ocular deviations are made in an inverse direction from that which we have just described if the lesions are irritative and not paralytic.

"It remains to explain some symptoms the interpretation of which, currently admitted, is not completely demonstrated by a sufficient number of autopsies. Among them, conjugate deviations from a lesion of the mesencephalon which for many are not sufficiently explained in spite of the laws of Grasset and Landouzy.

"Thus Prévost in 1900, in restudying conjugate deviation, affirmed that 'lesions of the pons which attack the nucleus of the sixth pair provoke a deviation of the ocular globes, not presenting the same characters as that which is observed in consequence of lesions of the encephalon.' The same thing is true, in our opinion, of the various forms of paralysis called the type of Foville, which are not all sufficiently explained, notably the inferior, by a sufficient number of autopsies. In many cases diffuse lesions are found in more of those to which the symptoms observed during life are attributed.

"By our schema other cases may be explained: A lesion at *Z*, at the point of crossing of the neurons of the oculogyres, will cause a double paralysis of divergence as in the case of Dor who, in speaking of this observation and of experiments made with prisms with the bases inward, affirmed that divergence is an active function opposed to convergence and not a relaxation of the latter, for one can neutralize a prism of 6 or 7 degrees by contraction of the external rectus.

"For an analogous reason, a lesion at *n*" at the decussation of the radicular fibers of the third pair, which act in associated convergence, would produce suppression or at least an enfeebling of the latter and, as a consequence, a divergent strabismus in the same way as a lesion at *Z* would produce a convergent strabismus.

"We consider the proposed schema only a working hypothesis, which can give rise to new investigations. It has, at least, the advantage of summing up in a

memotechnic fashion the principal physiologic and pathologic facts concerning the synergies of the internal rectus either with the opposite external rectus in the lateral gaze or with its homonym in convergence. To those who consider that to imagine schemas is to lose one's time, we will say with Hunter that isolated facts, however important and numerous they may be, never constitute science if one does not put them together in order to draw conclusions and to make general laws. We will have, at least, the advantage of fixing our ideas on this complex question."

DENNIS, Colorado Springs, Colo.

DISTURBANCES OF ASSOCIATED MOVEMENTS OF THE EYES. Q. DI MARZIO and G. FUMAROLA, Rev. d'oto-neuro-opht. **8**:299 (April) 1930.

This article, together with the one on laryngeal paralyses, occupies this entire number of the *Revue d'oto-neuro-ophtalmologie*. Di Marzio discusses the phenomena of associated eye movements and their paralytic disturbances, while Fumarola writes on the anatomy of the coordinating centers for movements of the eyes. These two dissertations are embraced in a report to the Fourth Congress of Oto-Neuro-Ophthalmic Societies held at Brussels in June, 1930. It is impossible to abstract such an article adequately without almost a complete translation, as it contains so many important details and comments on the rich literature of reported cases. Those interested are referred to the original article.

Di Marzio, after calling attention to the intimate association of movements of the two globes, refers to Parinaud's classification of associated eye movements into: "associated movements of direction" and "associated movements of distance." In making associated movements the globes pass from the primary position of repose to the secondary position in vertical and lateral movements and to the tertiary position in oblique movements. This requires the functioning of groups of muscles. When the eyes are turned horizontally to the right or left the associated movement involves only the internal and external recti muscles. When associated movements vertically up and down are made, the superior and inferior recti muscles are not sufficient, but must be supplemented by action of the oblique muscles: the inferior oblique for elevation and the superior oblique for depression of the globe. Oblique movements require the association of three pairs of muscles, two recti and one oblique. The movements of essential convergence require the action of each internal rectus; of asymmetric convergence laterally, the external rectus of one side with the internal rectus of the other, and for oblique convergence, the same groups of muscles that are involved in associated oblique movements. There are also associated movements of the intrinsic muscles, the associated movements of the iris and of accommodation. Again, there is association between the extrinsic and the intrinsic eye movements, as for example in convergence, in which the movements of the iris, of accommodation and of the internal recti are synergized. In order that simultaneous complex actions of several antagonistic muscles with different innervation may occur, more than one nuclear center must be concerned. There must be reciprocal relations of each nucleus of origin with all the others, with the visual center and with the cerebral cortex. The inhibitory action of the cortex also is necessary, being represented by the phenomena of relaxation and depression of the tonus of the antagonistic muscles. The tonus of agonists is increased while that of the antagonists is diminished. It is necessary to postulate distinct nerve pathways for motor impulses and for inhibitory impulses.

Disturbances of associated movements are divided into: disturbances of voluntary contraction of the agonists and those of inhibition of the antagonists, called "tonic disturbances." Velter's classification is: (*a*) tonic disturbances, which result from alterations of the regulator mechanism of tonus and of the nerve centers or the nerve pathways of the regulator apparatus; (*b*) paralytic troubles, which result from alterations of voluntary contraction dependent on a lesion of the corticonuclear pathway or of the peripheral system.

The neuromuscular ocular apparatus is subject to the laws of equilibration which control the motor system in repose as well as in action. The static equilibrium of the eyes may be disturbed, resulting in nystagmus, or the tonus of certain muscles may be exaggerated, causing an associated contracture. Kinetic equilibrium may likewise be affected through some defect of the apparatus of muscular tonicity, and this will be evident only during movement of the eyes. There results: oscillation in the eye movements, false positions of the eyes or incoordination of movements of the two eyes.

Barré described a "spontaneous nystagmus," a "revealed nystagmus," appearing when the eyes are turned to the sides or upward or downward, and a "provoked nystagmus," occurring from stimulation of the labyrinth. Spontaneous nystagmus in associated paralysis is a central reaction. It is frequently seen in multiple sclerosis and hereditary ataxia (appearing on voluntary movement), exceptionally in tabes and dementia paralytica and seldom in syringomyelia. In paralysis agitans it is simulated by the rigidity of the ocular muscles. In cerebellar lesions with nystagmus, Barré maintained that the vestibular pathways are always involved. It sometimes occurs in lesions of the quadrigeminate bodies, the bulb, pons, cerebral peduncles and optic thalamus. In cerebral lesions it is rarely seen and is associated with conjugate deviation of the eyes and rotation of the head to the side of the lesion.

Disturbed kinetic equilibrium is represented by spasm. Dejerine believed that many transient diplopias are better explained by contracture of one or several muscles than by paralysis. It is found frequently in cerebral diseases accompanied by conjugate deviation of the eyes; in paralysis agitans, which is accompanied by rigidity of the eye muscles and trembling, slowness of muscular action and false ptosis from spasm of the orbicularis, and Thomsen's disease (myotonia congenita). In some types of tabes there is hypertonus of convergence with homonymous diplopia.

In ataxia of the ocular globes there is oculomotor incoordination, which is sometimes clearcut, but usually the ataxia is latent and requires careful examination to elicit it. It is frequently found in tabes, and sometimes in Friedreich's disease and multiple sclerosis.

Paralysis of associated eye movements may involve either or both the intrinsic or the extrinsic musculature.

Paralysis of the external musculature is divided into: conjugate paralysis, in which oculomotor paralysis is associated with homonymous conjugate deviation of the head; simple associated paralysis, in which oculomotor disturbances exist without deviation of the head.

Four forms of paralysis of binocular movements were recognized by Parinaud: paralysis of parallel horizontal movements, paralysis of parallel vertical movements, paralysis of convergence and paralysis of divergence. Each of these forms may occur alone, but usually two or more co-exist. When associated paralysis of movements of laterality and verticality occur, diplopia is absent unless the degree of paralysis is not the same in the two eyes. Crossed diplopia always exists in paresis of convergence and, while the internal recti do not function in the attempt at convergence, the movements of laterality are normally executed. In paralysis of divergence, the eyes cannot be returned to a parallel position after convergence, and there exists an homonymous diplopia.

Most frequently a lesion of voluntary movements is accompanied by a lesion of the automatico-reflex movements. Disturbance of voluntary movements may exist without interference with automatico-reflex movements, but not the reverse.

Associated paralysis of laterality without conjugate deviation of the head is of great clinical importance because of its frequency, although it is rarely complete or equal in both eyes. It may be combined with paralysis of vertical movements or of convergence. Almost always paralysis of other cranial nerves or of the extremities is present also.

The paralysis of associated vertical movements was studied in detail by Parinaud and may be divided into four groups: paralysis of associated move-

ments of elevation, paralysis of associated movements ot depression, paralysis of associated movements of depression and elevation and associated paralysis of vertical movements complicated with other paralytic phenomena of the ocular muscles. They are seen frequently in an incomplete or atypical form.

In simple paralysis of convergence, accommodation and the pupillary reaction are conserved in the act of convergence, while in complete paralysis these are abolished. Associated paralysis of the two internal recti can exist with preservation of convergence. Likewise, there can be paralysis of the two oculomotors with normal convergence.

Convergent paralysis occurs in multiple sclerosis and asthenic paralysis and in lesions of the quadrigeminate bodies.

Paralysis of divergence is characterized by an homonymous diplopia with a short distance between the two images which persists in all directions. It may be combined with paralysis of convergence.

Later, Parinaud questioned the existence of divergent paralysis, attributing the phenomena to contracture of convergence. However, several other writers have published cases which speak for the hypothesis of divergent paralysis, though they were not supported by autopsy observations.

Numerous quotations from the literature, with critical comments, illustrating the various forms and combinations of associated paralysis are embodied in the report.

Fumarola, in his detailed anatomic consideration of the coordinating centers for eye movements, traces the known and postulated reflex arcs and pathways (association, corticofugal and corticopetal) of the various central nuclei with each other and with the cortical centers. Clinical facts supporting these anatomic facts are gathered from numerous sources. He shows the close functional connection of almost all the motor nerves of the face. He regards the mesencephalon as a superior reflex station. Pathologic lesions in such a narrow space, full of important centers and pathways, can rarely give specific localizing signs.

His conclusions are: "Disturbances of associated movements of the eyes can occur in consequence of lesions of very different localizations and situated especially: (*a*) in the cortical or subcortical region of the frontal lobe and of the inferior parietal lobe (gyrus supramarginalis and angularis); (*b*) along the pathways of corticofugal projection, which from the pes pedunculi (under the name of aberrant fasciculi of the peduncular pathway) pass in the lemniscus taking part in the innervation of the intercalated system; (*c*) in the nuclei of the motor nerves of the eye, and probably (1) in the fan-shaped nucleus for associated eye movements downward; (*2*) in Darkschewitsch's nucleus for upward movements of the eyes and closure of the lids; (3) in the lateral group of the small cells of Fuse for associated movements of laterality, and (4) in the nucleus of Westphal-Edinger and of Perlia for the movements of convergence, accommodation and contraction of the pupils; (*d*) along the association pathways running in the posterior longitudinal bundle between the nuclei of the motor nerves of the eye and the nuclear chains of the other sensory and motor nerves of the bulb, pons and mesencephalon; (*e*) the existence of coordinating centers, regulators of associated movements of the ocular globes, placed outside of the nuclei of origin of the motor nerves of the eyes; that is, the existence of extranuclear centers seated in the area adjacent to the lamina quadrigemina is improbable."

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THE PATHOLOGY AND ROENTGEN-RAY TREATMENT OF SYRINGOMYELIA. L. J. CZERNY and J. I. HEINISMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:573 (June) 1930.

Raymond (1905) first introduced deep roentgen therapy in syringomyelia. Recently, Proust, Mallet and Colliez reported the treatment in four cases of syringomyelia with good results. Kejser reported fifty-three cases in which the patients were treated by the roentgen rays; in six cases the disease progressed further despite treatment; in fifteen cases there was a subjective and objective

improvement, and in eleven the condition remained stationary. Poussep (1926) suggested surgical treatment for syringomyelia. He reported favorable results in two cases in which he punctured the syringomyelic cavity and then drained them. His observations have not been confirmed by others.

Czerny and Heinismann report 124 cases of syringomyelia. Of these, 70 patients were treated by the roentgen rays, and were observed over a period of from two to five years. The ages of the patients varied from 12 to 60, the average age being from 25 to 40. There were 52 cases in males and 18 in females. The clinical picture varied considerably. In most instances the process was symmetrical, but was more pronounced on one side than on the other. The process in these 70 cases was localized as follows: 4 with cervical localization only, 39 of cervicothoracic involvement, 10 of cervicothoracicolumbar involvement, 1 of thoracicolumbosacral involvement and 2 in the thoracic cord. In 12 cases the medulla was involved in addition to the cord, and in 2 cases the diencephalon was implicated. Schlesinger said that the medulla is involved in one third of all cases of syringomyelia. He found it involved in 9 of 19 cases. Czerny and Heinismann found the medulla involved in 12 cases, or 17.1 per cent. In syringobulbia only from the fifth to the twelfth cranial nerves are involved. Schlesinger explained the involvement of the first four cranial nerves on the basis of an accidental complication, or as the result of basal inflammation. Matsumato found the olfactorius involved in 15 per cent of all cases of syringobulbia. There was anosmia in two of the cases reported herein.

Schlesinger had never seen spasmodic laughing and crying in any of his cases, but Czerny and Heinismann report such an instance which was improved with roentgen treatments. In only one case were changes found in the eyegrounds. Primary atrophy in syringomyelia is mentioned in the literature, independent of any accidental complications. Maixner found an optic atrophy in three of thirty-two cases. The origin of this atrophy is not clear. In Czerny's case there was also microphthalmia, nystagmus and symmetrical syndactylism. In 8 per cent of the cases there was paralysis of the extra-ocular muscles.

Nystagmus is often the only symptom that points to a supramedullary involvement. Haenel emphasized the fact that in many cases the nystagmus is not part of the syringomyelia but a developmental anomaly that runs parallel with the hydrocephalus that is present. Matsumato reported six cases with nystagmus. According to Schlesinger, nystagmus occurs in 15 per cent of all cases of syringomyelia. Leidler has shown that the cause of the nystagmus lies in an injury of the spinal roots of the auditory nerves, that is, of those fibers passing to the posterior longitudinal bundle. Nystagmus was present in 12.8 per cent of the cases of Czerny and Heinismann. In more than half of these cases there was other evidence of bulbar involvement. Rotary nystagmus occurred more often than other forms. Nystagmus was often helped by roentgen therapy.

The motor root of the trigeminal nerve is rarely involved. Three cases are reported in this series. The sensory root of the trigeminus was often involved. The sensory disturbances were of a dissociated nature; pain and heat were disturbed. Trigeminal pain may exist for years as the only sign of a syringomyelia.

Roentgen treatment caused a definite improvement of the pain and paresthesias in syringomyelia. Often the former was worse after the first treatment, but then gradually subsided. Striking improvements were noted in the objective sensory pictures. Recession of the sensory changes could be followed after successive treatments. Improvement was first noted in the sensation of pain, and then in temperature. An improvement in the sensation of touch has thus far been noted in only one case. A complete recovery from sensory loss was rare. The improvement was first noted in the segment that represented the lowest portion of the cavity. In the majority of cases the improvement could be followed gradually, first in the trunk and lower extremities and then in the upper limbs. Czerny and Heinismann interpret this to mean that the process is most recent in the lower part of the cord. The improvement in sensation follows the clinical picture in its recession.

Motor disturbances were found in 95 per cent of the cases. In 52 per cent there was flaccid paresis of the upper extremities, and in 25 per cent flaccid paresis of the upper extremities and a spastic paralysis of the lower extremities. Amyotrophies were most common in distal segments and less common in proximal segments. In thirteen cases ataxic phenomena were present. Cases of isolated ataxia without paresis and atrophy of the extremities were not observed. Improvement in the motor symptoms was common. The muscle power increased from 14 to 20 Kg. by dynamometer, the hypertonia disappeared, the gait improved and the patients could walk much farther. There was also an increase in the range of movements. In one case there was paresis and atrophy of the shoulder girdle with marked limitation of movement. After two series of roentgen treatments over a course of three months there was a complete recurrence in the range of movement. Tremors of the hands improved after roentgen treatments. In many cases lost reflexes reappeared. In the reappearance of the reflexes, there first occurred fibrillary twitchings, then movements of muscle segments and finally the appearance of the reflex.

It is well known that vasomotor and trophic disturbances often occur in syringomyelia, and this series is no exception to this observation. Acrocyanosis, hyperkeratosis, thickening of the skin and trophoneurotic dermatoses were seen. Under the influence of roentgen therapy, the cyanosis and coldness of the extremities disappear, and the hyperkeratoses soften. In many cases the eczema disappeared. Gangrene of the skin was observed in three cases, and this condition improved with roentgen therapy.

The joints and bones are involved in from 20 to 25 per cent of cases of syringomyelia, according to Schlesinger, and in 10 per cent according to Ssokalow. Arthropathies may be the earliest symptom of the disease. Some authors describe pure arthritic forms. Czerny and Heinismann found that many cases of subluxations, deforming arthritides and chronic joint troubles had their origin in a syringomyelia. In their cases pain often preceded the condition of the joints. The elbow and shoulder joints are most often involved, after them the hands. The typical bony change in syringomyelia consists of bone atrophy which usually gives no clinical symptoms. In the long bones there is usually decalcification at the epiphysis. Hypertrophic changes also occur, but less often than atrophic changes, and they are usually due to ossificatoin of a proliferated periosteum. Kyphoscoliosis often occurs; it is often the only early symptom in youths and in children. In such cases the syringomyelia may remain latent for years. In a case of Foix and Faton's the kyphoscoliosis was observed when the patient was 14 years of age and the other symptoms of syringomyelia appeared after the age of 15 years. The kyphoscoliosis was cervicodorsal in 54 per cent of the cases here reported. An improvement in six cases of bone atrophy was noted after roentgen treatment.

Although sluggish and Argyll Robertson pupils occur in syringomyelia, this is not well known. Deformities of the pupils are common in the presence of a good light reaction. In 11 per cent of cases there was a sluggish reaction of the pupils to light and convergence. Horner's syndrome occurs in 15 per cent of cases of syringomyelia. In this series of cases it occurred in 50 per cent, more often unilateral, but often bilateral.

ALPERS, Philadelphia.

COMPLETE SOFTENING OF BOTH CEREBRAL HEMISPHERES IN AN INFANT AGED TWO MONTHS. F. SCHOB, J. f. Psychol. u. Neurol. **40**:365 (May) 1930.

Within a few hours after birth, an infant was admitted to the Municipal Hospital in Dresden with its mother, who was suffering from florid secondary syphilis. The infant was born at full term, was strong and well developed and was without visible signs of syphilis; it was 51 cm. in length; the circumference of the cranium was 36 cm., and its weight was 3,250 Gm. A Wassermann reaction of the blood taken seven days after admission was negative. The infant was breast fed and increased steadily in weight until the thirty-sixth day after admission, when a tem-

perature of 38 C. (100.4 F.) and loose green stools developed. During the next three days, with the persistence of the diarrhea and the fever the appetite became poor, and the infant began to lose weight. On the thirty-ninth day, there appeared tonic seizures of the muscles of the neck and of all four extremities. During these seizures, which lasted from one-half to one minute, the face appeared bluish red and the head was held in extension and to the right with deviation of both eyes to the same side. Any attempt to rotate the head to the left was followed by a spontaneous rotation back to the right. The legs were in flexion, and passive extension met with great resistance and was apparently painful. At times the left palpebral fissure was wider than the right; at other times the right was wider than the left. The pupils were equal in size and reacted to light. There was no nystagmus and no Chvostek sign. The deep reflexes were normal.

Although the infant showed no evidences of syphilis, owing to the mother's severe syphilitic infection, it was subjected to three prophylactic injections of sodium arsphenamine (0.0225 Gm.). The fever, however, as well as the seizures, loss of appetite, diarrhea and loss of weight persisted till the fifty-fifth day after admission when the seizures ceased. During the next ten days the infant was semicomatose and marasmic; it died on the sixty-fifth day after birth.

Necropsy revealed a high degree of marasmus, complete absence of fat and evidences of severe gastro-enteritis. The viscera, meninges, blood vessels and cranial nerves were normal. Both cerebral hemispheres appeared like two flabby bags; the external configuration of the brain was still recognizable although the convolutions felt soft. The entire surface of the brain was of a light yellowish tinge. On horizontal section there exuded from both hemispheres a grayish-yellow, pastelike, fatty, fluid substance. After washing out this fluid the entire white substance of both hemispheres seemed to have disappeared in some areas, while the remaining areas were soft so that the entire brain was replaced by a cavity that was traversed by a network of the cerebral vessels. The parts of the central ganglia adjacent to the walls of the ventricles also seemed to have participated in the softening. The cerebellum, crura cerebri, medulla oblongata and spinal cord showed no gross abnormalities.

Histologic examination revealed an extensive nonpurulent process consisting of a chronic inflammation of the pia, with numerous lymphocytes and plasma cells, and of small nodular granulations around the vessels and in the substance of the brain and cerebellum. These granulations appeared as focal nodules and consisted partly of fibroblasts and partly of glia cells interspersed with plasma cells. Although spirochetes could not be demonstrated in any of the tissues, the presence of small granulomas consisting of giant cells and of plasma cell infiltrations and the positive history of syphilis in the mother led the author to regard the condition as one of meningo-encephalomyelitis syphilitica congenita (Ranke).

Although Schob makes this diagnosis, he raises the question whether the softening was actually due to congenital syphilis. He is certain that it could not have been due to endarteritic changes with closure of the vessels by thrombi because such vascular changes were not found on histologic examination. Whether or not such softening could have been produced by the toxin of syphilis is not definitely known, although it is common knowledge that, for example, in dementia paralytica in adults there may occur less marked softenings in the brain in the form of a status spongiosus of the cerebral cortex. Nor is it definitely known whether or not the immature tissues of the new-born infant may not react to such toxins more readily than the mature tissues of the adult. Schob is also unable to exclude positively the possibility of trauma to the brain during birth which in the presence of syphilis may subsequently give rise to more advanced softenings in the traumatized areas. Finally, it may also be possible, as the first cerebral manifestations (the seizures) appeared simultaneously with the onset of gastro-intestinal disturbances, that toxins from the latter cooperating with an already existing injury to the cerebral tissue and vascular apparatus from syphilis could also produce such severe lesions in the brain. In this connection the author also points out the impossibility of determining definitely whether or not the gastro-

intestinal symptoms could be regarded as a secondary general manifestation of severe disease of the brain.

Schob thus shows that in spite of the progress of knowledge of the effects of cerebral birth trauma there is little positive knowledge of the etiology and genesis of cerebral softenings in the new-born infant and of porencephalus in general. In a previous communication he had already shown that by far the greater number of porencephalies begin during intra-uterine life, before the completion of the sixth embryonal month, because many of these porencephalies are associated with malformations, such as microgyria and heterotopies, which could only have developed before the sixth embryonal month. He admits, however, that it is not at all rare to encounter cases of porencephaly that apparently had not appeared until a considerable period after birth. The etiology and genesis of these cases still await explanation.

KESCHNER, New York.

SYRINGOMYELIA WITH UNILATERAL SYRINGOBULBIA. VELOPALATOLARYNGOPHARYNGEAL PARALYSIS, CLOCKWISE ROTATORY NYSTAGMUS. ANDRÉ-THOMAS and C. KUDELSKI, Rev. d'oto-neuro-opht. **8**:377 (May) 1930.

A married woman, aged 40, entered the hospital complaining of violent crises of pain in the base of the thorax, arm, the neck and the frontal region of the same side (left?). The duration of the crises was a few minutes, and they were not very frequent. At the end of three months, the gait was impaired. After about one year improvement began, and the patient returned to work; but shortly afterward the pains recurred, and she was again treated in the hospital with improvement for a time when the symptoms returned once more. Examination revealed thickening of the cellular tissue and skin of the entire left arm and side of the face, hyperextensibility of the flexors and extensors of the hand and fingers and of the brachial triceps. The left shoulder was less freely movable than the right, but a roentgenogram showed no lesion. Muscular force in the muscles of the shoulder and arm was not diminished, but there was a diminution of electric excitability in most of them. Active or passive movements of the affected parts were painful; there were spontaneous movements of the hand, the arm and the shoulder, resulting in instability of the left arm. This state of agitation was accentuated by movements of the right arm, by loud noises or by pricking the right concha, but it was not increased by voluntary movements. Incoordination, but not adiadokokinesis, existed. All reflexes in the left arm were abolished. The left leg was thrust forward in extension during walking, the point of the toes was carried outward and the heel was put down sharply. There was incoordination but no dysmetria. The gait was still uncertain, and the body oscillated in walking. Power was not diminished in the muscles of the leg and toes, but was a little less in the flexors and extensors. The left thigh was smaller than the right, and extensibility of the quadriceps was greater on the left. There was pain in the left hip and stiffening of the thigh, which did not occur so frequently as in the arm. The achilles reflex was abolished on the left and the patella reflex was feeble. On the right side the reflexes were lively, and there were clonus of the patella and a slight clonus of the foot. The cutaneous abdominal reflex was normal on the right and feeble on the left side.

Sensibility was intact on the right side. On the left, touch was almost normally perceived on the arm and thorax, except on the hand and the lower part of the forearm where it was feeble. There was complete anesthesia to pricking and to heat and cold in the whole left arm, on the thorax to the median line and below to the mamillary line in front and the inferior angle of the scapula behind; on the neck in the domain of the cervical plexus; on the ear, sparing the concha and the posterior wall of the meatus. Deep sensibility was likewise affected. There was astereognosis. In the left lower extremity, superficial sensibility was preserved. Articular sensibility was markedly altered in the toes, the tibiotarsal, the knee and the hip joints.

The masseter reflex was lively on both sides, but the corneal reflex was diminished on the left. The pupils were equal and reacted well to light and in convergence. There was a clockwise rotatory nystagmus, increased by looking laterally, more on looking to the left.

The palate deviated to the right and was more elevated on the right in phonation or in the pharyngeal reflex. The left posterior pillar contracted more feebly than the right. The pharynx was displaced to the right (sign of Vernet). The left vocal cord was paralyzed, but there was no atrophy. The left arytenoid preserved a slight seesaw movement on phonation. Sensibility of the left half of the palate, the epiglottis and the larynx was diminished. Hearing was normal. There were some sensations of vertigo.

After two minutes' irrigation of the right ear with cold water, the direction of the nystagmus was not changed, but the jerks were wider and slower on looking to the left; there was slight past-pointing. After three minutes, there was intense vertigo and deviation to the right. On irrigation of the left ear, nystagmus in the same direction, but quicker, was noted. There was a past-pointing to the left and a marked vertigo. In the oculocardiac reflex test, the pulse rate dropped from 112 to 104.

This case presents a spinobulbar syndrome. The spinal element consists in unilateral disturbances of sensibility and motility; the latter is represented by ataxia with no paralyses or atrophy. These disturbances are allied to lesions of the long fibers of the posterior columns and to disorders of deep sensibilities. The pains and dissociation of the anesthesia in the left upper extremity indicate a lesion of the posterior horn and the radicular fibers which terminate there. The bulbar syndrome consists principally in a velopalatolaryngopharyngeal paralysis with hypesthesia, rotatory nystagmus, diminution of the corneal reflex and exaggeration of the masseter reflex. Particular attention is called to the clockwise rotatory nystagmus. This is a frequent sign in low bulbar lesions, left-sided lesions causing a clockwise and right-sided lesions an anticlockwise nystagmus.

The loss of the achilles reflex and diminution of the patella reflex indicate an extended lesion of the cord (lumbar region). Exaggeration of the tendon reflexes in the right leg is caused by either a lesion in the lumbar region or a lesion of the crossed fibers of the motor pathway at the collet of the bulb.

This form of syringomyelia and syringobulbia is remarkable on account of the unilaterality of the symptoms, of the nature of the disturbances of motility, the velopalatopharyngeal paralysis and the rotatory nystagmus.

DENNIS, Colorado Springs, Colo.

PERIARTERITIS NODOSA WITH SEVERE INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM. W. RUNGE and R. MELZER, J. f. Psychol. u. Neurol. **40**:298 (May) 1930.

A divorced man, aged 61, with an unfavorable social history, was operated on for gastric ulcer at 54. Three years later, atrophy of the left leg, an unsteady gait, and a dysarthric speech developed. His physician attributed these symptoms to a previous apoplexy. Two years later, he was unable to dress himself, his nutrition became impaired and he had two episodes of gastric distress and persistent vomiting. At this time he was admitted to a hospital where the condition was considered one of cerebral vascular disease and adhesions following laparotomy. At about the same time he was also treated for suppurative thrombophlebitis.

When he came under the observation of the authors, he showed a syndrome referable to involvement of various cerebral and peripheral systems: (1) complete paralysis of the tongue, and bilateral facial diplegia; (2) extrapyramidal symptoms —pseudospontaneous involuntary athetoid movements, increased during mental excitement, and striking changes in muscle tonus, ticlike muscular contractions and abnormal associated movements; (3) marked ataxia on intention; (4) pyramidal tract signs on the right side; (5) possibly central visual disturbances (hemianopia?); (6) atrophy of the left lower limb, due to involvement either of the

anterior horn cells or of the peripheral nerves; (7) mental symptoms—marked apathy with periodic restlessness suggestive of cortical involvement; it was impossible to determine whether or not he had an outspoken dementia. Sensation could not be tested. There was a diastolic murmur at the apex of the heart; the pulse rate was 64 and regular; the systolic blood pressure was 145. The urine was normal, although during one of the episodes of gastric distress mentioned it was of high specific gravity and contained urobilinogen, leukocytes, erythrocytes, hyaline and granular casts. The serology and cytology of the blood and spinal fluid were practically normal. The neurologic symptoms and signs persisted; the general nutrition became very poor, and he died four years after the onset of the nervous symptoms from inanition and obstinate vomiting.

Necropsy revealed: adhesive pleurisy, thin cardiac valves, brown degeneration of the myocardium, saccular dilatations of the anterior and posterior walls of the left ventricle, moderate coronary sclerosis, moderately severe sclerosis of the aorta and chronic gastric and duodenal ulcer. The liver was small and smooth; on section it appeared reddish brown and its markings were indistinct. The pancreas was small and narrow, and the spleen was contracted and hard in consistency, with a pale bluish-red, wrinkled capsule, with definite markings of the trabeculae. Both kidneys were small and their capsules adherent; their surfaces were finely granular and full of coarse scars; on section they appeared pale reddish brown, with a very narrow cortex. The thyroid was small and contained a moderate amount of colloid material.

The brain weighed 1,255 Gm.; the dura was relaxed and the pia diffusely thickened over both convexities and adherent to the underlying cortex. The accessory sinuses were normal, and the hypophysis small and dirty grayish brown. The arteries at the base of the brain showed "spotty" sclerotic deposits without gross narrowing of their lumina, except for the vertebral artery which contained a completely occluding thrombus, 2 cm. in length, about 1 cm. before its juncture with the basilar artery. The irregularity of the surface relief of the brain was striking even macroscopically. Normal convolutions of the brain alternated with abnormally narrow ones, especially in the left occipital lobe. In some areas the surface of the brain showed scar formation. The affected convolutions had a softer texture than those surrounding them. On frontal section the cerebral cortex and part of the underlying white substance showed brownish discoloration. The entire cortex appeared moth-eaten and spongy. No abnormalities were observed in the basal ganglia.

The lower portion of the cervical spinal cord had a softer texture than the remaining portions of the cord, but the dura was not adherent. On section, this part of the cord showed a slightly patchy reddening of the gray matter with areas of dirty grayish discoloration and softening of the posterior columns. Similar changes were observed in the lumbar portion of the cord.

Histologic examination revealed most unusual changes in the blood vessels of the internal organs and central nervous system. These changes may be summarized as: (1) involvement of the media and intima with a normal adventitia leading frequently either to complete closure or to a marked narrowing of the vessel lumen, and (2) a formation of thrombi in various stages of organization. There were no evidences of an inflammatory process in the vicinity of the vessels. It was noteworthy that this systemic disease of the vessels involved not only the various internal organs (especially the heart and kidneys) but also the brain. The architectonic structure of the cerebral cortex as well as of the subcortex showed severe alterations, with areas of destruction in the presence of well preserved basal ganglia. The areas of destruction showed evidences of marked pathologic changes of the ganglion cells and glia in addition to products of degeneration. The pathologic process throughout the brain was apparently due to changes in the blood vessels and corresponded to the anatomic distribution of the latter. Similar changes were also found in the cerebellum (in the form of atrophy of the cerebellar lobe), olive, dentate nucleus, internal capsule and lateral columns of the cord.

In the differential diagnosis of the vascular changes in this case the authors considered the following possibilities: periarteritis nodosa, arteriosclerosis, Heubner's obliterating endarteritis and syphilitic endarteritis of the small cerebral cortical vessels (Nissl-Alzheimer).

The only arteriosclerotic changes found macroscopically in this case were those in the large blood vessels. Microscopic examination of the internal organs and of the pial vessels showed neither degenerative changes in the intima nor hyaline calcifications in the media. Syphilitic endarteritis could be excluded, because in this disease vascular changes in the brain can be found only in the small pial and cortical vessels. Formation of new vessels with dilatation and formation of pockets, a condition usually observed in syphilitic endarteritis, was not observed in the case under discussion.

It was much more difficult, however, to differentiate periarteritis nodosa from Heubner's obliterating endarteritis. Characteristic of the latter are the proliferative changes in the intima and, in contrast to arteriosclerosis, the fairly regular absence of evidences of breaking down of the new formations in the intima. Arteriosclerotic cases, on the other hand, also show inflammatory changes, lymphocytes and plasma cells in the adventitia, which, according to Spielmeyer, initiate the pathologic process in the vessels. In some of the sections examined in the case under discussion areas were found that resembled the histologic picture of Heubner's endarteritis, but there were no evidences of any infiltrative inflammatory process in the adventitia, no new formation of elastic fibers in the intima, no aneurysmal dilatations and no giant cells. Neither did the sections show any other characteristics of syphilitic vascular disease such as gummas or caseation. Many sections taken from the cortex were stained for spirochetes, but none were found. In this connection it must also be stressed that there was no history of syphilis; the serology of the blood and cerebrospinal fluid was negative, and there were no pathologic evidences of syphilis in any of the other organs.

In view of all these facts the authors regard this case as one of periarteritis nodosa — a systemic disease of the vessels characterized by involvement of the media and intima, with preservation of the adventitia, without inflammatory infiltrates in the tissues adjacent to the vessels, and with secondary thromboses in various stages of organization. The extensive and severe changes in the central nervous system are regarded as sequelae of the lesions in the blood vessels. In their opinion the entire pathologic process is an expression of the cicatricial stage of periarteritis nodosa.

KESCHNER, New York.

NEUROLOGY AND PSYCHIATRY IN HYPOGLYCEMIC STATES. JOSEF WILDER, Med. Klin. **26**:616 (April 25) 1930.

Since the use of insulin, spontaneous and artificial hypoglycemia has become so frequent that Wilder calls attention to the condition, especially from the neurologic and psychiatric standpoints. If one injects insulin into a rabbit sufficient to lower the blood sugar below 45 mg. per hundred cubic centimeters, the animal develops convulsions. All animals do not react in the same way; sheep, especially, are refractory to insulin. The attacks usually appear in from one and one-half to two hours after the injection. Just what precipitates the convulsions remains a question, but it is a clinical fact that the ingestion of sugar gives immediate relief. It is worthy of note that in decerebrated animals insulin produces no change in the blood sugar and convulsions do not occur. With excessive use of insulin, changes in the nerve cells and axis cylinders have been observed, but it must be remembered that similar changes have been found in diabetic persons in whom insulin has not been used.

Most of the observations on hypoglycemia have been made by the internist, the neurologist only rarely making a contribution to the subject. There is a great individual susceptibility to insulin, so that there is no rule regarding the amount of insulin that may be used. Approximately, when the blood sugar is under 70 mg., hypoglycemic symptoms may occur, and above 80 mg., they are rare.

Hypoglycemic symptoms are essentially of nervous origin and may produce vegetative, central nervous system or psychic phenomena. The rather light vegetative attacks are frequent. They are made up of fatigue, sleepiness, hunger, sweating, pallor, tremor, chills, acroparesthesias, salivation, nausea, etc. Associated with this group, the mild symptoms of the central nervous system may also be noticed, as slight incoordination and even psychic changes may be present: restlessness, anxiety, irritability, light depression and even slight mental cloudiness. According to Oppenheim, the vegetative symptoms occur within from one to two hours after the injection. The symptoms of the central nervous system usually occur later. The maximum effect of insulin occurs about three hours after the injection. To understand the vegetative symptoms one must remember that insulin is a vagotrophic hormone that acts through the vagus and that the symptoms are not unlike the vagotonia of Eppinger.

The severe hypoglycemic symptoms of the type of those of the central nervous system, which are found in about 1 per cent of diabetic persons, may occur insidiously or may come on suddenly. Headache, scotomas and double vision are frequent forerunners of an attack. The speech becomes slow, difficult and slurred; the tone changes, and megaphonia may appear. There may occur emotional laughter and crying. Marked restlessness or motor agitation may supervene. Very often the patient will feel the onset of an attack and say, "Now I must eat sugar," but on failing to do so more severe symptoms develop. The symptoms are somewhat akin to mescal delirium. An interesting fact is that during the lighter forms of the delirium the patient is able to describe clearly his subjective sensations. From a psychologic standpoint the condition is especially worthy of study, as a prompt reversibility of the attack is constantly at one's disposal. Marked negativism may be present. Sullenness, anger and all other symptoms disappear suddenly with the taking of a little sugar and water.

Severe collapse or even attacks of unconsciousness may occur; they are especially important as they may be associated with cerebral or arachnoid bleeding, which may lead to death. Since the use of insulin, the occurrence of transient hemiplegias, transient blindness and other apoplectic forms of symptoms has been observed, especially in the more severe arteriosclerotic types of the disease. These conditions have been explained on the basis of a cerebral angiospasm. In the more specific hypoglycemic attacks there may be severe coma, which may last from hours to days, ending spontaneously or resulting in death. At times the stupor suggests a catatonic state. The patient may even answer questions on recovering from the attack, stating that he heard everything that was said but was unable to move or talk. For this reason it is difficult to ascertain if there was a true loss of consciousness, for soon after the attack, there may be a complete amnesia. The amnesia is one of a constant type of symptoms in the severe attacks. Rarely, illusions may be present during attacks, and, as a rule, the patient does not recall the incident following recovery.

Another phenomenon associated with the more severe attacks is motor unrest. This may be confined to one muscle, a group or the entire body; even generalized convulsions have occurred. The author states, however, that he has never seen a true epileptic attack, as biting of the tongue. Associated with the more severe attack, there may be transient ocular palsies, fixed pupils, absent reflexes and the Babinski sign, all of which again disappear under sugar therapy.

In the psychotic group there may be states resembling epileptic stupor. The patient may lose himself. There may be impulsive acts; even suicide or homicide may occur. Manic pictures may exist. There may be singing, jumping, laughing, etc. Frequently, these patients resemble hysterical persons. Apparently, the prepsychotic personality plays no rôle in the development of the symptoms. In differential diagnosis, epilepsy is especially to be thought of. If there is a history of diabetes or the use of insulin, the diagnosis is easy. In a spontaneous hypoglycemic attack, the diagnosis is more difficult; in a doubtful case, sugar therapy should be instituted. In spontaneous hypoglycemia there is a fairly constant history. At first, the attacks occur at long intervals; gradually they appear every week, and

finally, several times a day. They steadily become more severe and finally lead to coma or even death, the entire course being a matter of several years. As a rule, one may obtain a history of the association of the attacks with the intake of food and yet, surprisingly frequently, these patients are considered neurasthenic.

Hypoglycemic attacks of endogenous origin may result from various causes, as adenoma of the islands of Langerhans, severe diseases of the liver, Addison's disease and possibly also hypothyroidism. Renal diabetes may also play a rôle. To this already large group, the author adds a group that he has described under the heading of hypophyseal spontaneous hypoglycemia. He reports two such cases, in both of which the sella was enlarged and thinned. Wilder believes that frequent hypoglycemic attacks occur in hypophyseal cachexia but that they are overlooked because of the other more profound symptoms. The group of hypophyseal hypoglycemic attacks is as yet not clearly established, but the author wishes to include it at this time to stimulate attention to the condition.

MOERSCH, Rochester, Minn.

THE CHIASMAL SYNDROME OF PRIMARY OPTIC ATROPHY AND BITEMPORAL DEFECTS IN ADULTS WITH A NORMAL SELLA TURCICA. HARVEY CUSHING, Arch. Ophth. **3**:505 (May); 707 (June) 1930.

This article, an address before the International Congress of Ophthalmology in 1929, was brought up to date and amplified for publication in the *Archives of Ophthalmology*. It is a consideration of the chiasmal syndrome in which the sella turcica remains, relatively speaking, unaffected. From an ophthalmologic standpoint, its value is to assist in a djagnosis, so that, to quote Dr. Cushing, "the advantage to a surgeon in knowing with reasonable certainty before opening the skull not only the situation of the lesion he is to attack but its precise histological nature," and "one might suppose, in view of the experience already gained with the syndrome in question, that fewer diagnostic mistakes would occur." The article is subdivided into sections based on the various lesions found, for example, the suprasellar meningiomas, the suprasellar adenomas, craniopharyngiomas, gliomas of the chiasm, suprasellar aneurysms, a rare chordoma with a suprasellar syndrome and this chiasmal syndrome in the absence of a tumor.

The article is based on a special study of 186 cases with a total mortality of approximately 10 per cent, regardless of the type of lesion encountered. Differential diagnosis and mistaken diagnoses, as confirmed at the operation, are given bare consideration in this review. The same applies to the description of the pathologic changes of each type of lesion as it is outlined in the article. Each section is clearly illustrated with case records, anatomic drawings and photographs and with the all important visual fields in the cases included in the text. The operations are described. The postoperative notes in each case are included, with a reviewing comment for each section.

In none of the cases of suprasellar meningiomas has there been any symptomatic evidence of recurrence (thirteen years being the longest time since operation). The article points out that the syndrome of the suprasellar adenomas simulates closely that of the meningiomas, except that the adenomas usually give greater evidence of pressure with more rapid progress of the symptoms and with a co-existence of mild hypopituitary signs. Relative to the craniopharyngiomas, Dr. Cushing states that in spite of the most variable and protean constitutional defects produced by this tumor, it is the easiest of all the intracranial tumors to diagnose. He emphasizes its congenital anlagen, its almost universal though variable degree of calcification and its occasional secondary pituitary and hypothalamic disturbances, and by reason of its close chiasmal anatomic relationships, the marked frequency of chiasmal symptomatology. In regard to the chiasmal gliomas, he mentions and emphasizes the average age of the patient in the group (14 years), the frequent associated evidences of generalized neurofibromatosis, the more bizarre field defects, the rare appearance of hemianopia with a vertical meridian and the occasional papilledema due to the spread of the glioma down

the length of the optic nerve. The frequent involvement of the wall of the third ventricle and its resulting hydrocephalus are also stated. In the section in which the author considers suprasellar aneurysms, he comments on their strangely silent or almost bruitless nature, on the value of this point in differential diagnosis, on the frequency with which these aneurysms rupture before diagnosis is made, the probability of accompanying arterial hypertension, the symptomatology from the standpoint of other cranial anatomic relationships and the difficulties in their surgical treatment. A rare tumor, the chordoma with a suprasellar syndrome, was 1 of only 3 instances in a histologically verified series of 1,800 tumors. The cases with a chiasmal syndrome in the absence of tumor are explained on the basis of a chronic arachnoiditis having an excess of fluid, when through operation there was a failure to find a tumor mass. Nasal accessory sinus disease is considered as another possible cause for the syndrome.

In the final summary of the paper the author discusses certain points which will be reviewed here more in detail. In considering the character of the primary optic nerve atrophy he states that "it is sometimes difficult to tell whether atrophy is present or not." In one case, quoted in full, the attending ophthalmologist was unwilling to state definitely that an atrophy was present unless he had a contralateral fundus for comparison. Relative to the bitemporal character and progress of the field defects, Dr. Cushing thinks that their interpretation is without doubt of much greater diagnostic value in suprasellar lesions than are any changes in the eyegrounds, "important as these may be." The defects progress unequally, and the unilateral or bilateral onset of the blindness depends on chiasmal pressure wherein one nerve may be thrown wholly out of function before any pressure or stretching has occurred in the opposite nerve. He pleads for more accurate perimetric work. He hesitates, as a surgeon, to make such a criticism, but his experience in neurosurgery has demonstrated the necessity for accurate quantitative perimetry.

The author discusses the normality of the sella turcica from the standpoint of a problem for roentgenologists. The sharpening of the anterior clinoid processes, the angulation and the degree of thinning of the dorsum sellae, evidences of changes in the sulcus chiasmatis, and changes in the optic foramina and in the general form and position of the nonexpanded sella all need detailed study.

In conclusion, the single outstanding differential point for each type of lesion is quoted, the relationship between the neurosurgeon and the ophthalmologist is emphasized and a retrospect is given of the adenomas and those tumors which arise from the anlagen of Rathke's duct, the operability of the meningiomas and lastly that this syndrome of the adenomas, the chiasmal gliomas, the meningiomas and the craniopharyngiomas can be simulated as well by certain other conditions, "which with further study should be capable of clinical differentiation without the necessity of an exploratory operation."

SPAETH, Philadelphia.

HEADACHES OF NASAL ORIGIN, PARTICULARLY SPHENOIDAL HEADACHES. GEORGES CANUYT, Rev. d'oto-neuro-opht. **7**:567 (Oct.) 1929.

The past nasal history in patients with headaches of nasal origin is important. Questioning will bring out the fact that they have suffered from frequent coryzas, and that the headaches began after an unusually acute cold. They are divided into anterior and posterior headaches. The former are caused by hypertrophy of the head of the inferior turbinates, deviations, ridges or spurs of the septum, compression from hypertrophy of the middle turbinate, obstruction of the naso-frontal duct or infections of the frontal, anterior ethmoidal or maxillary sinuses. The posterior headaches are caused by mechanical or infectious agents seated in the posterior ethmoidal cells, the ethmosphenoidal recess and especially the sphenoidal sinus.

Anterior headaches from acute frontomaxillary sinusitis are described in detail. Certain symptoms are emphasized: the exact localization of the pain, usually supra-orbital, pain on moving the eyes and the periodicity of the headache. The pain frequently comes on at a definite hour, rapidly increases in intensity, and

after two or more hours remits to return again next day. Rarely are there two paroxysms a day. The periorbital region and the teeth are sensitive to pressure, the area over the exits of the supra-orbital and infra-orbital nerves particularly. The interior of the nose is swollen and tender, closing the region of the middle meatus. All of these patients have narrow nasal passages. After eight or ten days, the nasal congestion diminishes, pus appears under the middle turbinate and the headaches subside. Relief is afforded by the application of a solution of cocaine-epinephrine under the middle turbinate. In cases in which this means fails, resort is had to blocking the internal nasal and supra-orbital nerves with procaine-hydrochloride.

In chronic cases there is usually meatal obstruction of the nasofrontal duct or an ethmofrontal mucocele. The pain is increased by close application of the vision as in reading or sewing, the insertion of the pulley of the superior oblique muscle (Ewing's point) is tender, the nose is narrow and there is compression of the middle turbinate region by hypertrophy, polyps, septal deviations, etc.

Mucocele usually begins in the ethmoid cells and extends later to the frontal sinus. In its ethmoidal stage of development it is possible in certain cases to recognize it: unilateral pain in the frontal region and at the internal angle of the eye, which is tenacious and severe and occurs in crises that are intolerable. The most valuable aid in the diagnosis is the roentgenogram. The sinuses involved are cloudy, and the bony walls of the ethmoid cells, the orbit and the interfrontal sinus septum lack sharpness of shadow. The therapy is largely surgical.

In posterior headaches, the posterior ethmoidal and sphenoidal sinuses are clinically considered as one. Usually the patients are young women who have suffered with tenacious persistent headache for years. They often give evidence of neurasthenia. They complain of a deep pain in the center of the head, in the occiput, behind the eyes or in the nasopharynx. Many of them have pain in the neck and in the vertex, and both physical and mental activity is difficult or impossible. These cases require complete and often repeated clinical examinations to determine the etiology. The rhinologic examination must be thorough and should include the use of the nasopharyngoscope, catheterism or puncture of the sphenoidal sinus, transillumination and roentgenography. Catheterization of the sphenoid and percussion of its posterior wall is regarded as an important diagnostic measure in posterior headaches. Good results have been obtained from physical therapy: infra-red rays, high frequency and diathermy. Cocainization of the sphenopalatine and the sphenoidal sinus followed by cauterization with silver nitrate has given excellent results. Various surgical procedures, ranging from scarification of the inferior turbinate and puncture of the sphenoidal sinus to exenteration of the ethmoid labyrinth and wide opening of the sphenoidal sinus, are recommended.

In headaches the chief difficulty is accurate diagnosis. Many cases will tax the resources of the internist, the neurologist, the ophthalmologist and the rhinologist working in cooperation.

DENNIS, Colorado Springs, Colo.

RESEARCHES IN FEEBLE-MINDEDNESS WITH SPECIAL REFERENCE TO INHERITANCE. ABRAHAM MYERSON, Bull. Massachusetts Dept. Ment. Dis. **14**:109 (April) 1930.

The rôle of heredity in the development of feeblemindedness has, Myerson believes, been greatly exaggerated. While it is true that the families of institutionalized, mental defective patients show a greater percentage of feeblemindedness than the families of the ordinary school child, this proportion is weighted by the fact that it is largely the mental defective children whose families are incompetent and unable to care for them who become institutionalized. Furthermore, the historians in most schools and asylums for the mentally deficient are content to accept vague evidences of such traits as "queerness" and "delinquency" as proof of psychopathic heredity without much critical investigation. Myerson admits that even with these subtractions a large number remain wherein feeblemindedness in ancestors seems to be followed by feeblemindedness in children. But this, he

insists, is still no proof of the absolutely congenital nature of such defects — first, because the very bad training to which a child in a family of mentally deficient persons would naturally be subject would in itself handicap the development of normal intelligence, and second because there is no reason to assume that inherited qualities are permanently isolated from the influence of environment. We are, he affirms, too prone to think that the germ plasm lies in an impenetrable capsule and too unwilling to recognize that changes in nourishment and nerve supply may modify the gene. He cites biologic evidence that serious environmental changes can modify the germ plasm enough to start a new line of "inherited characteristics." For this reason he believes that if instead of despairing because of an orthodox concept of "poor protoplasm" one tried to give the plasm as congenial an environment as possible one would be making real progress. From a statistical point of view, feeblemindedness acts like a mendelian simple recessive trait. He investigated several families in which there were mentally defective persons, criminals, and social problems of all sorts, and he emphasizes the fact that even the worst of these had normal collateral branches, and that the feeble-minded persons from such families came out of a most unfavorable environment. He also cites evidence to show that the importance of feeblemindedness as a factor in crime has been exaggerated. He vigorously assails the polymorphic theory of heredity, i. e., the idea that all sorts of unrelated mental, nervous and physical disorders, such as epilepsy, achondroplasia, feeblemindedness, insanity, etc., together constitute a neuropathic unit, and that the existence of any of these in a family tree stigmatizes the family as neuropathic. He is inclined to emphasize the importance of injury at birth and infection in the development of feeblemindedness. He considers each type of feeblemindedness, the cretin, the mongolian, the hydrocephalic and microcephalic, the syphilitic and the idiopathic, and shows that for all except the last group, heredity certainly plays no rôle; while unprejudiced study of the family histories of many of the idiopathic mental defectives shows a strong tendency to assign a neuropathic heredity on meager evidence. He concludes by expressing the belief that if one took the children with unfavorable heredity and placed them in a favorable environment, one would be happily surprised at the result. The entire paper is a vigorous expression of Myerson's faith in the great importance of environment.

DAVIDSON, Newark, N. J.

THE EMOTIONAL BEHAVIOR OF YOUNG CHILDREN DURING MENTAL TESTS. FLORENCE L. GOODENOUGH, J. Juvenile Research **13**:204 (July) 1929.

Goodenough studied emotional traits in behavior during the psychometric examination of 990 children between the ages of 18 months and 6 years. It was found possible by the use of descriptive categories to classify the behavior in a highly objective manner. The data thus obtained was correlated with age, sex, social status as indicated by paternal occupation, and position in the family. A decided improvement in behavior with increasing age was found for each of the three traits. In boys this improvement did not begin until about the age of 30 months, while girls showed steady improvement from 18 months on. The boys were rated as slightly more negativistic and distractible than the girls, while no sex difference was apparent as regards shyness. The mean ratings on shyness for the boys of the lower social classes were significantly lower (indicating less shyness) than those for the girls of corresponding social status, or those of either sex from the upper social classes.

The boys of the upper social classes were rated as much more negativistic than those of the lower classes. Among the upper social classes the boys were rated as more negativistic than the girls; among the lower social classes the girls were slightly more negativistic than the boys. The ratings on distractibility are higher (indicating greater tendency to distraction) for boys than for girls at each social level, and higher for the upper than for the lower social classes for both sexes.

"Only" children were on the average rated as somewhat less shy and very much more distractible than children in families of more than one child. The

difference is most marked when the comparison is made with children who are the oldest in their families.

The correlations between the mean ratings on the same trait for a group of 72 children of 2 years of age, who were given a second test after an average interval of 42.6 weeks, show a sufficient degree of consistency over the shorter interval to indicate that the behavior shown is, for the time being, fairly characteristic of the individual in the type of situation under consideration.

The author concludes that these facts, taken in conjunction with the differences existing between children occupying different positions in the family group and with the reversal of the sex differences in regard to negativism for children of different social classes, point to the conclusion that the individual differences in behavior revealed by these ratings are more attributable to differences in training and experience than to innate tendencies.

PEARSON, Philadelphia.

THE REACTION OF BRAIN TISSUE TO THE INTRAVENOUS INJECTION OF HYPOTONIC SOLUTIONS. ARMANDO FERRARO, J. Nerv. & Ment. Dis. **71**:129 (Feb.) 1930.

L. H. Weed was the first to use an intravenous injection of hypotonic solutions in physiologic experiments on cerebrospinal fluid. The use of these solutions for therapeutic purposes suggests the necessity of investigating the changes in the brain produced by them. Histologic changes have been reported by Forbes, Fremont-Smith, Cobb, Kubie, and Penfield; they consist of swelling in the cells of the choroid plexus and hydration of the central nervous system. The author gave intravenous injections of distilled water in amounts of from 35 cc. to a global dose of 950 cc. at twenty-four hour intervals to sixteen rabbits. Microscopically, he found swollen brains with rounded bulging frontal and occipital poles, and an almost complete obliteration of the fissures and furrows. By means of hematoxylin-eosin, Bielschowsky, Plein, Spielmeyer, van Gieson, Cajal and Hortega technics he has observed the following histologic changes: the subarachnoid spaces were constricted; the ventricles and central canal of the cord appeared dilated; the ependymal cells showed disruption, shrinking and impaired colorability; karyolysis of the nuclei and subependymal edema were also demonstrated. The changes in the choroid plexus were earliest in development. The effects of ether are less outspoken and inconstant, and therefore these changes could not be attributed to the use of ether in killing the animals. Loosening and swelling of the interstitial tissue was noted mostly in the white fibers of the pes pedunculi, Ammon's horn and the optic tract. Grapelike areas of disintegration were seen in the internal capsule and Ammon's horn. Widely dilated perivascular and perineuronal spaces, particularly in the basal ganglia, were observed. Weed and Kubie did not find evidences of intracellular hydration to the extent that does the author, perhaps because of the latter's use of distilled water in larger quantities. In some instances he found vacuolization of the cell body with disintegration and loss of staining power and also vacuolar degeneration of the nuclei, with loss of nuclear chromatin. Nerve fibers may show hydration with swelling of the myelin sheaths. Astrocytes are not affected by small amounts of water, but after repeated and considerable injections they may show acute clasmatodendrosis. The microglia showed swelling as well as the oligodendroglia. The blood vessels of larger caliber showed no pathologic changes, but there was evident swelling without degenerative changes in the lining epithelial cells of the smaller vessels and capillaries.

HART, Greenwich, Conn.

CEREBRAL TUBERCULOSIS, INTRACRANIAL HYPERTENSION AND PAPILLARY STASIS. D. MANOLESCO and D. LAZARESKO, Rev. d'oto-neuro-opht. **8**:382 (May) 1930.

This observation concerns a boy, aged 19, who four years previously had suffered from a cranial trauma. In October, 1926, there were hemoptyses. Since January,

1927, the patient complained of frontal headaches; diplopia appeared later and vision failed, at first in the right eye. In June, the patient appeared for examination with the symptoms of vomiting, headache and blindness.

Examination revealed unequal pupils, abolished light reflex, feeble pupillary reaction to convergence and bilateral papillary stasis. There were paralysis of the right motor oculi, left hemiparesis without modification of tonus, slight bilateral cerebellar phenomena and absence of automatic movements and sensory disturbances. There was hypo-excitability of both labyrinths with loss of reaction from the left vertical canals. The tension of the spinal fluid was 72 (Claude) in the horizontal position.

The diagnosis was tumor of the right hemisphere, compressing the internal capsule. A temporoparietal decompression relieved the headache and vomiting temporarily, but within a few days the patient became worse and died two months later.

Autopsy revealed two fairly large tumors in the right lenticular region. The internal capsule and the head of the caudate nucleus were not involved. The median and right lateral ventricles were compressed and displaced to the left, and the left lateral ventricle was dilated. Through the anterior perforated space, the chiasm and right optic nerve were compressed. A similar tumor was found in the left cerebellar hemisphere. All tumors were tuberculomas.

The left hemiplegia is explained by the tumors in the right capsulostriate region and the bilateral cerebellar phenomena by pressure on the dentorubric fibers by compression from both groups of tumors. Aside from a slight trembling and the absence of automatic movements, there was no sign of parkinsonism.

On admission, the patient was blind, but no optic atrophy was noted. It is probable that direct pressure from the neoplasm on the optic tracts was added to the stasis in the sheaths of the optic nerves, especially since the history showed first failure of vision in the right eye.

DENNIS, Colorado Springs, Colo.

EXPERIMENTAL AND CRITICAL CONTRIBUTION TO THE KNOWLEDGE OF THE GRANULES IN THE GANGLION CELLS OF THE CENTRAL NERVOUS SYSTEM. NAOMITSU SUZUKI, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:163 (May) 1930.

Normal ganglion cells in the nervous system contain the following types of granules: Nissl bodies or tigroid substance, and Altmann granules (Held's neurosomes or mitochondria). More inconstant granules are found in the brown pigments. Pathologic granules that have been described are: Negri bodies, Babes' bodies, Koch-Rissling coccus-like formations, Nissl's ringlets, Alzheimer's fuchsinophil granules, Alzheimer's light green granules, Nissl's incrustation processes, Spielmeyer's degeneration bodies, etc.

Suzuki reports his investigations into these various types of granules except the Nissl bodies, the brown pigments and the fat granules. He has found that the ganglion cell reacts to a noxious stimulus by the appearance of fine and coarse granules in the nucleus. The former are normal, but are increased in amount in pathologic conditions; the latter appear only in pathologic states. These granules wander to the periphery of the nucleus. The coarse granules have a double structure; their inner portion takes an acid stain and their peripheral portion a basophilic stain. The fine granules are basophilic, but granules of a little larger size have an acidophilic and basophilic structure. These granules arise from the nucleolus. Suzuki has investigated in particular the structure of the Negri bodies. It is thought that these bodies are specific for rabies. He has found, however, that the so-called Negri bodies are merely derivatives of the newly formed nucleoli and granules in the ganglion cell nucleus as the result of noxious stimuli. Like the nucleoli they show both an acidophilic and a basophilic structure, and they occur not only in rabies but also in various toxic and infectious diseases. According to Suzuki, the Negri bodies and the Alzheimer fuchsinophil granules are absolutely identical. He states also that Negri bodies never occur during the latent stage

of rabies. The ringlets described by Nissl are also acidophilic and basophilic in structure, and are related to the granules described.

Suzuki believes that in reality there are not a great number of granules; they can all be grouped into one system.

ALPERS, Philadelphia.

THE PROBLEM OF THE ACUTE ENCEPHALITIDES. E. M. WIESEN, Arch. f. Psychiat. **90**:46, 1930.

The author reports four cases of acute encephalitis. Case 1 was that of a woman, aged 21, with a pronounced chorea which developed after a febrile angina and led to death. Histologically, paravascular infiltrations were found in the basal ganglia and in the brachia conjunctiva.

In case 2, a sudden apoplectiform attack developed in a woman, aged 35, following an apparently uneventful childbirth. The course was acute, and the patient died two days after the onset. Histologically, there was a diffuse small-cell infiltration of the pia and a mild infiltration of isolated vessels in the cortex and white matter. Case 3 was that of a man, aged 25, who was given Pasteur treatment after having been bitten by a dog. Following the injection a pronounced general reaction with unconsciousness developed. There were no neurologic signs except inequality of the pupils and trismus. Toward the end, a general absence of reflexes was found. A diagnosis of meningo-encephalitis was made. Histologically, a pronounced congestion of the vessels and a small-cell infiltration of the vessel walls in the medulla oblongata were found. Case 4 was that of a woman, aged 36, who had an attack of influenza with general symptoms; following this palsies of the eye muscles, weakness of the seventh nerve and disturbance of swallowing developed. Histologically, an acute encephalitis was found.

The author discusses the four cases, especially with reference to the controversy between Pette and Spielmeyer, and comes to the following conclusions: (1) The rapid course and poor prognosis of certain forms of acute encephalitis seem to depend on the extent to which the whole organism is affected by the infection. (2) The symptom-complex of the neurologic aspect of the clinical picture does not always correspond to the character and localization of the pathologic involvement of the brain. (3) The apparent cause of this incongruity must be looked for in the condition of organs outside the central nervous system.

MALAMUD, Iowa City.

THE PROBLEM OF THE ACTION OF COLORS ON THE ORGANISM. K. GOLDSTEIN and O. ROSENTHAL, Schweiz. Arch. f. Neurol. u. Psychiat. **26**:3, 1930.

It has long been known that mental tonus is modified by vestibular, acoustic and optic stimuli as well as by those of proprioceptive origin. Goldstein has found this demonstrated especially well in patients with frontal and cerebellar lesions. In this paper the authors report the results of studies of the effect of visual stimuli in the form of various colors.

Without exception, red and yellow were found to increase the spontaneous outward deviation of the outstretched arms of patients with cerebellar or frontal lobe lesions, while blue and green had the opposite effect. In the first instance the movements were smooth and gliding as the influence of the optic stimuli coincided with the spontaneous tendency, while the movements that occurred when the subjects looked at green objects were inclined to be jerky, since the tendency to outward deviation was opposed by the effect of the stimulus. Observations were also made on the influence of color on the subject's estimation of speed of movement, location of cutaneous stimuli and weight of objects, the results coinciding more or less with those already given.

The authors regard these phenomena as physiologic. They are not purely physical, for when the subjects looked at a given color until it appeared gray or black under the influence of fatigue the movements of deviation ceased; they

also do not depend on previous psychic experiences, for the invisible ultrared and ultraviolet rays were also found to influence deviation. The psychic effects of the colors, as expressed by the patients, were more or less in accord with those expressed by well known authors. In general, red and yellow stimulated, while blue and green exerted a restful influence. The authors believe that this demonstrates the narrow relation existing between psychic and corporal functions and the importance of observations of tonus changes in the study of mental phenomena. In closing, the authors suggest that studies such as theirs might aid in the proper selection of colors for the sickroom.

DANIELS, Rochester, Minn.

HYPNOTIC INHIBITION AND MÜLLER'S PHENOMENA. A. KARATAMISHEV and H. LEVITT, Mod. Neuropsychiatry (Kieff) **11**:55, 1930.

Müller demonstrated that following an intradermal injection of milk, water or air there is a drop of leukocytes in the peripheral circulation. This is due to irritation of the vagus, which causes a vasodilatation of the blood vessels in the splanchnic area. This leads to the increase in the number of leukocytes in the visceral area with consequent diminution of white cells in the peripheral circulation. In other words, the leukopenia is a reflex. The skin is a receptor in the reflex arc and must be in a healthy condition. The authors ask themselves the following question: As hypnosis is an inhibitory agent in the central nervous system, would there be, under the influence of hypnosis, an interruption of the reflex arc with consequent absence of a leukopenia after intradermal injections?

Twenty-two patients were studied, and fifty-one experiments were made. In four cases after hypnosis, no leukopenia appeared after intradermal injections of saline solution. Variations up to 2,000 cells were not considered significant, because this number was within the range of experimental error. Leukopenia took place in the same patients when they were not hypnotized. The factor of the pain produced by the injection was studied. It was found that deep hypnosis causes an analgesia. Painful stimuli were applied in the form of intradermal injections of ether, but leukopenia did not appear. The authors refer to Pavlov's theory according to which mental diseases, especially schizophrenia, suggest states of profound inhibition such as one may find following hypnosis. In the two cases of catatonic stupor which the authors studied Müller's phenomenon could not be elicited, probably owing to the already mentioned inhibitions of the central nervous system. On the other hand, the phenomenon was positive in paranoic persons.

KASANIN, Boston.

THE ENERGY EXPENDED IN MAINTAINING A MUSCULAR CONTRACTION. D. W. BRONK, J. Physiol. **69**:307 (May) 1930.

Bronk studied the economy of energy expenditure in maintaining muscular contractions at various frequencies of stimulation and in progressive fatigue. This was done by measuring the heat production and the tension-time. It was found that as the rate of stimulation is increased, the economy, or amount of tension-time maintained per unit of energy expended, increases. This is largely due to a greater degree of fusion of the separate muscle twitches, there being no further increase in economy with frequencies of a value higher than that needed to produce complete tetanus.

These results are discussed in relation to the observations of Adrian and Bronk, which show an increased strength of muscular contraction to be due in part to an increase in frequency of motor excitation. It may therefore be concluded that tension is maintained at a smaller expenditure of energy in a strong contraction than in a weak one. At 0 C. the increase in economy develops at lower frequencies. In cold-blooded animals this factor would be of significance in the event that the range of frequency of impulses from the motor centers was lowered as a result

of a fall in temperature. A stimulation frequency not quite sufficient to give partial summation of the successive twitches will, if continued, produce a fused tetanus.

Associated with this changed condition of the muscle there is a greater economy of maintaining tension. It is pointed out that this factor may play an important rôle in long sustained contractions in which there would be reason for expecting a decreased frequency of motor impulses.

ALPERS, Philadelphia.

PSYCHIC TROUBLES FROM THE USE OF HASHISH. FAHREDDIN KERIM, Encéphale **25**:93 (April) 1930.

These studies are presented from the Neuropsychiatric Institute and the Faculty of Medicine of Constantinople. The illicit traffic in hashish is discussed; likewise its increasing employment is indicated. Users are believed to be fundamentally psychopathic and of feeble will power; frequently they consume other drugs simultaneously. In such persons imagination is excessive; repugnance to all types of work is extreme; there exists a strong inclination to solitude; intelligence may be very good. As to the effects of the drug, although varying with the personality of the individual patient, the following general statement can be made: The intoxication induces a lassitude and peculiar nonchalance; the volitional field is retracted; association of ideas is lessened and even interrupted; imagination is exalted and plunges into all sorts of dreams and intense revery. Later, all sense of time and place is lost. Some patients become violent and delirious; they may commit criminal acts. Incoordinate movements, profound depression, and extreme physical and mental sluggishness are often manifested. All of these symptoms may merge gradually into a chronic state, with certain organic alterations: anemia, increased tendon reflexes, tachycardia, dyspnea, etc. The principal psychic syndromes observed in inveterate users are: (1) Cerebral erethism, with all the rapidity of thought and morbid gaiety characterizing a manic state; (2) a subacute melancholia; (3) dementia praecox, the syndrome most frequently encountered (disturbances of emotion, impulsive acts, and weakness of memory and attention are characteristic), and (4) mental confusion, with complete disorientation, panophobia and hallucinations. Citations of cases illustrate each of these types.

ANDERSON, Los Angeles.

THE PSYCHIATRIST IN SOCIAL WORK. FRED J. FARNELL, J. Nerv. & Ment. Dis. **71**:397 (April) 1930.

The greatest foe to successful work in social service is stereotopy and automatism. Lawyers are slaves to precedent, and the medical profession dislikes innovations; similarly the social worker who reacts in the same manner to each case is less valuable than one who sees the manifold possibilities and remedies. Routinism and lack of coordination in the field of the social sciences are the present serious defects. Too much is expended by the state on its wards in proportion to the amount of return, which it interests both the state and individual to increase. The population of our state institutions is increasing with the danger of reducing the capacity of individuals to produce and to adapt themselves. It is a mark of merit to keep some one out of an institution and not to commit him, which is a sign of failure. Psychologic tests approach the problem from only one point of view leaving out the personality, emotions, interests and skill. Close intensive cooperation between the psychiatrist, the psychologist and the social worker is vital. Sterilization of feebleminded girls thus enabling them to earn their living in society without becoming a social liability is to be recommended in preference to institutionalization. Energy and money have been wasted in useless sentimentality with the ultimate deprivation of the individual patient, and unbusinesslike methods are adopted in groundless fear of efficiency. The social worker's task is to secure progress by overcoming ignorance, error and pessimism and to weld the forces of progress into some degree of harmony.

HART, Greenwich, Conn.

EXPERIMENTAL AND PATHOLOGIC STUDIES OF THE EPENDYMA AND CHOROID PLEXUS. C. T. VAN VALKENBURG, Monatschr. f. Psychiat. u. Neurol. **74**: 133 (Dec.) 1929.

In the first part of this article the author investigates the ependymal cells lining the central canal of the spinal cord. In diseases such as poliomyelitis, Landry's paralysis, syphilitic meningomyelitis and amyotrophic lateral sclerosis he observed regressive and productive changes of a primary nature in these cells. Similar changes were produced in rabbits by injecting various substances into the region of the central canal. Here, too, the ependymal lesions occurred independently of neighboring neuroglial reactions.

In the second section, the author directs attention to the choroid plexus and the ependymal cells lining the ventricular cavities. In the latter he was unable to produce proliferative changes by experimental means. In purulent infections of the cerebrospinal fluid, he found that the ependyma was completely destroyed in some places, but only moderately affected in others. It showed no alterations in nonpurulent infections. As a rule the choroidal cells were less involved than the ependymal elements. Regardless of whether the ependymal cells were intact or not, the author observed perivascular infiltrations of leukocytes extending for a distance of from 2 to 3 mm. into the tissues lining the ventricular cavities. This did not occur in the choroid plexus or other parts of the brain. He concludes that the choroid plexus offers more effective resistance to the spread of infectious products present in the ventricular fluid than does the ependyma.

ROTHSCHILD, Foxborough, Mass.

A STUDY OF ALAMEDA COUNTY DELINQUENT BOYS WITH SPECIAL EMPHASIS UPON THE GROUP COMING FROM BROKEN HOMES. SARAH B. CROSBY, J. Juvenile Research **13**:220 (July) 1929.

Crosby analyzed the case records of 314 delinquent boys in regard to their home conditions. She found that among these juvenile delinquents broken homes appear in all probability much more frequently than among the population of the county as a whole. The frequency of broken homes is estimated to be almost twice as great in the delinquent group as in the population at large. The greater number, or 71.3 per cent, of the delinquent boys coming from broken homes were from homes broken by the absence of the father. Of the boys from 12 to 16 years of age, the greater number came from complete homes.

In regard to charges listed against the boys, crimes against property, "disturbing the peace" and violation of the state motor vehicle acts and ordinances were more frequent against boys from complete homes. The charges indicating a lack of personal and self control (incorrigibility, rape, truancy and "danger of leading an idle, dissolute and immoral life") were found more frequently against boys from broken homes.

The author concludes that home conditions of the boys who have both parents may be no more satisfactory than the conditions found in broken homes. Home conditions of the boys from broken homes, generally, are not considered by the probation officers so satisfactory as the home conditions found among the group of boys who have both parents. The boy who lacks a father often faces a psychologic and economic situation that is too serious for the boy himself to meet satisfactorily.

PEARSON, Philadelphia.

POSTPUNCTURE HEADACHES. MARQUE O. NELSON, Arch. Dermat. & Syph. **21**:615 (April) 1930.

The usual assignment of leakage as the cause of postpuncture headache is confirmed by Nelson in a series of biologic and clinical experiments. He found a general incidence of 20 per cent for headache following a spinal tap, and a 10 per cent incidence in sufferers from neurosyphilis. Evidence that leakage was

the responsible factor was afforded by a study of spinal pressures during the attack of headache and a demonstration that these were uniformly low. This, Nelson believes, is due to the small amount of fluid present which, in turn, is due to leakage. The relief of headache in a recumbent position is further evidence of the importance of this agency. A final confirmation of the opinion, as well as a suggestion for relief of the symptom, is afforded by Nelson's method of plugging the dural trap door with catgut. This is inserted through the cannula of the needle and retained by a special instrument. In cases in which this was done the puncture headache incidence fell to 5 per cent; it remained at 20 per cent in the group of patients not treated in this way. Experimental work on dogs, in which catgut was inserted through the needle in a similar way, the dogs being subsequently submitted to autopsy, demonstrated that the catgut first became swollen and effectually plugged the dural opening; subsequently it became absorbed without residue. Nelson's final conclusions are that postpuncture headache may be diminished by discouraging leakage, and that leakage may be definitely reduced by plugging the meningeal opening with sterile catgut inserted through the needle.

DAVIDSON, Newark, N. J.

THE RESULTS OF THE TREATMENT FOR EPILEPSY WITH BRAIN EMULSION. M. N. STAWROWSKAJA, Monatschr. f. Psychiat. u. Neurol. **74**:221 (Dec.) 1929.

For several years the author has been employing emulsion of the brain in the treatment for epilepsy. The material is prepared from the brains of rabbits under strictly aseptic conditions. The skull is opened, and the brain removed. The latter is weighed and cut into small pieces. Ten times its weight of physiologic solution of sodium chloride is added drop by drop, the brain tissue being ground down until an emulsion is formed. This is filtered through a fine metal sieve, and as a rule injected into the patients at once. If necessary, it can be preserved in an ice box for two or three days. It is given subcutaneously, 1 cc. being injected daily for thirty days. After an interval of a month, the course is repeated. In some cases the injections were continued for two months, the treatment then being interrupted for a similar period. As a rule, from three to five courses were given to each patient. Sixty ambulatory patients were treated and observed over a period of three years. The number of seizures was diminished in 86.7 per cent of the cases. In 20 per cent of the cases the seizures disappeared completely. No unpleasant complications were observed, although at the beginning of the course some patients exhibited a temporary increase in the frequency and severity of the attacks. Some patients required sedatives during the periods when the treatment was interrupted. The author believes that the general condition of practically all of the patients was improved. This was shown by an increased appetite, a better capacity for work, an improvement in memory and a general feeling of well being.

ROTHSCHILD, Foxborough, Mass.

SUPERSTITIONS OF COLLEGE STUDENTS. R. GILLILAND, J. Abnorm. Psychol. **24**: 472 (Jan.-March) 1930.

That a person has fewer superstitions after taking a psychology course than he had before is one of the conclusions that Gilliland draws after his analysis of superstitions in a class of liberal art students, and in an evening class of commercial students. Out of a list of thirty superstitions, his college class, taken as an average, expressed faith in ten; after finishing their psychology course, they adhered to only six of these superstitions. The commercial class showed an improvement of from twelve articles of faith before the course to only six at the end of the study. Some of the statements presented are not universally accepted as superstitions, however. In this investigation the student who believed that

"intelligence can be improved by training" was considered the victim of a superstition on the subject, and the same stigma was attached to the one who thought that "man is superior to animals because he is guided by reason."

DAVIDSON, Newark, N. J.

BRAIN FUNCTIONS. EDITORIAL, J. A. M. A. **95**:1268 (Oct. 25) 1930.

Cerebral localization is as yet far from determined. For a century or more the pendulum has swung from one extreme to the other. Flourens taught that the cerebrum is a single organ, in all parts functionally equivalent. Soon the cerebrum came to be regarded as a "plurality of organs." Howell has pointed out recently that the cerebrum is very intimately connected histologically and physiologically. Animal experiments are difficult to interpret in the human light. Dandy, of Johns Hopkins University, has reached the following conclusions: The right hemisphere may be removed with no appreciable disturbance of mentality. Both frontal lobes have been removed with no appreciable disturbance of mentality. Excision of the left occipital lobe and of the lower third of the left temporal lobe produced no effect on intelligence. Consciousness is completely and forever lost after ligation of the left anterior cerebral artery but not when the right one is ligated. The entire body of the corpus callosum may be split in the midline without appreciable disturbance of function.

CHAMBERS, Syracuse, N. Y.

OCULAR ASPECTS OF CONDITIONED REFLEXES. T. H. EAMES, Arch. Ophth. **3**:758 (June) 1930.

The literature of conditioned reflexes is unfortunately sparse when one considers only the number of writers — not the content of their writings. This article is a rather interesting one of the ocular relationship of such reflexes. Many of the aspects quoted by the author are by no means new but when based on this physiologic reaction, all of them appear in an interestingly new light. Even the homely fact of the ophthalmologists' substitution of a Windsor chair for the usual dentist-like ophthalmic chair is to be considered seriously. As stated in the article, "the extent to which associated stimuli and conditioned reflexes occur in connection with the eyes is greater than might be supposed. A few of them have been mentioned . . . but the systematic analyst can discover them in every ocular function." This statement should clarify etiology in some instances and explain certain symptoms in others, and, when considered carefully, should assist appreciably in rational therapy.

SPAETH, Philadelphia.

ALLERGIC MIGRAINE: BASED ON THE STUDY OF FIFTY-FIVE CASES. RAY M. BALYEAT and FANNIE LOU BRITTAIN, Am. J. M. Sc. **180**:212 (Aug.) 1930.

Heredity is one of the most important factors in the production of migraine as is shown by a positive family history of allergy in 85.4 per cent and a family history of migraine in 45.4 per cent in the fifty-five cases of migraine studied. The exciting factor is always a specific sensitivity to one or more foreign proteins, and multiple sensitivity is the rule. Physical fatigue, mental fatigue, depressed states, thyroid dysfunction, genitosexual causes, toxic states and disturbance of the special senses are predisposing factors. Five cases are cited as illustrations of the aforementioned points. In one third of the cases the onset occurred in the first decade, and in 12.7 per cent symptoms persisted until the sixth decade. Good results can be expected only when the exciting factor, namely, the foods to which the patients are specially sensitive, is removed.

MICHAELS, Detroit.

THE THROMBOCYTES IN PERNICIOUS ANEMIA. A. KRISTENSON, Upsala läkaref. förh. **35**:185, 1930.

According to Kristenson, a study of the number of thrombocytes can yield valuable prognostic information in pernicious anemia. A constantly low or decreasing number of blood platelets indicates a bad prognosis. When their

number reaches about 5,000, the prognosis is very bad. Gradually increasing numbers justify a better prognosis. During a remission the increase in the number of thrombocytes begins earlier than the increase in erythrocytes and assumes the character of a hemoblastic crisis. Therapy (arsenic and iron, diet of liver, blood transfusions, etc.) has no noticeable effect on the character of the reaction of the blood platelets. Hemorrhagic diatheses and a low number of thrombocytes are not necessarily associated with each other. These conclusions have been reached from seventeen cases of pernicious anemia in which repeated determinations of the red and white blood cells, of the blood platelets and of the hemoglobin percentages were made.

KESCHNER, New York.

LATE FORMS OF FAMILIAL PROGRESSIVE MYOPATHY. K. H. KRABBE, J. Neurol. & Psychopath. **10**:289 (April) 1930.

Krabbe discusses the age incidence of the myopathies and points out that those which develop late usually do not present a familial history, while in 50 per cent of cases developing early in life, there is a familial history. He reviews about twenty cases from the literature that developed after the age of 30. In only two of these was there a history of similar conditions in the family. He reports two cases of his own, one in detail and one casually. The patients were sisters, and in both the condition developed at about 45 years of age. In both the condition was limited to the lower part of the legs; in one a biopsy was performed and showed a replacement of muscular by adipose tissue; Krabbe did not attempt to classify this case in any of the known groups.

ROBINSON, Kansas City, Mo.

EXOPHTHALMIC GOITER: THE PROTEIN CONTENT OF THE SPINAL FLUID. W. O. THOMPSON and B. ALEXANDER, Arch. Int. Med. **45**:122 (Jan.) 1930.

Observing the high protein concentration in the spinal fluid of myxedematous patients, Thompson reasoned that there should be a low protein content in the fluid of patients with exophthalmic goiter. A study of fifteen patients with this condition revealed an average protein concentration of 24 mg. per cubic centimeter —within the lower limits of normal. After subtotal thyroidectomy the concentration rose in all but one case, the average concentration being 37 mg. per cubic centimeter. While the authors express uncertainty about the cause, they advance the suggestion that the nitrogen substance store is reduced in hyperthyroidism.

SPINAL CORD INJURY. GEORGE G. DAVIS and H. C. VORIS, Arch. Surg. **20**:145 (Jan.) 1930.

In demonstration of the fact that dislocation of a vertebra may cause permanent cord damage, even though subsequent reduction of the luxation results in normal x-ray pictures; Davis and Voris present a case. The patient fell from a height of 30 feet and landed on the buttocks. There were signs of a transverse lesion of the cord at the level of the third or fourth cervical segment. Roentgen examination showed nothing definite. The patient died, apparently of an ascending pyelitis, and postmortem examination showed a hematomyelia. Davis and Voris believe that the compression itself, apart from hemorrhage, was responsible for some of the symptomatology.

BEHAVIOR DISORDERS IN CHRONIC EPIDEMIC ENCEPHALITIS. CHARLES E. GIBBS, Am. J. Psychiat. **9**:619 (Jan.) 1930.

After considering the symptomatic differences between the behavior of the constitutional psychopathic and the postencephalitic child, Gibbs concludes that the conduct disorder of the latter is the product of genuine organic cerebral pathology, probably thalamic. The functional association of the thalamus with

the affective mechanisms, and the emotional disturbance that would follow thalamic disease, seem to be the responsible factors. A realization that the process is of inflammatory nature would suggest some degree of therapeutic optimism.

PSYCHOPATHOLOGY OF ALCOHOLISM. WILLIAM D. TAIT, J. Abnorm. Psychol. **24**: 482 (Jan.-March) 1930.

In this paper Tait eventually reached the profound conclusion that people drink alcoholic liquors because they make the world look rosy to them. Alcohol, he said, solves our conflicts, makes us lords of creation for the time being and resolves our troubles. He expressed the belief that compensation for sorrows of the day is a corollary reason. The paper concludes with the presentation of the cases of three respectable citizens who engaged in alcoholic debauches to compensate for the crushing sobriety of their normal lives.

THE RESPONSE TO PLANTAR STIMULATION IN INFANCY. L. V. WOLFF, Am. J. Dis. Child. **39**:1176 (June) 1930.

In the first few months of life, the most usual response to plantar stimulation is not the classic Babinski extension of the great toe, but a dorsal extension of all the toes. In a small percentage of new-born children, plantar flexion occurs; this group increases in size as age advances. By the fifth month, almost half of the infants in Wolff's series showed flexion. As this occurred before the child could walk, the mechanism of plantar flexion cannot be concerned with the process of walking.

DAVIDSON, Newark, N. J.

THE ISOMETRIC RESPONSES OF MAMMALIAN MUSCLES. SYBIL COOPER AND J. C. ECCLES, J. Physiol. **69**:377 (June) 1930.

By means of a frictionless myograph, the mechanical isometric responses of mammalian muscles with diverse "contraction times" were investigated by Cooper and Eccles. It was found that the responses of the muscles, both to two stimuli at various intervals and to repetitive stimuli at various rates, show similarities if the time intervals are measured relative to the respective "contraction times"; but the ratio of the maximum tetanus tension to the twitch tension is usually greater for muscles having a short "contraction time." The relation between the rate of stimulation and tetanus tension follows an S-shaped curve for all the muscles studied.

THE PATHOLOGY AND CLINICAL ASPECTS OF THE MENINGIOMAS. ERICH GUTTMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **123**:606 (Jan.) 1930.

Guttmann found 48 meningiomas among 11,000 autopsies. These he divides arbitrarily into meningiomas the size of a cherry, plum and hen's egg, and larger tumors. Of his meningiomas, 38 occurred in women and 9 in men. The tumors were most numerous from the fifth to the eighth decade. The average age was 42½ years. In 4 cases there was a pachymeningitis hemorrhagica. Bony changes were found in 16 cases; in 14 cases there was erosion, and in only 2 cases hyperostosis.

ALPERS, Philadelphia.

TUMOR OF THE FOURTH VENTRICLE SHOWING DEVIATION OF THE HEAD AS THE ONLY SIGN. KNUD WINTHER, Acta psychiat. et neurol. **5**:45, 1930.

Winther reports a case of atsrocytoma fibrillara of the wall of the fourth ventricle. The initial symptom was vomiting, and sudden movements of the head produced vertigo. Later, the head was held in forward flexion and turned to the left. Any attempt to change this position produced vertigo. The author believes that the position of the head was maintained because it caused the tumor to produce the least interference with the circulation of the cerebrospinal fluid.

PEARSON, Philadelphia.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Annual Meeting, May 23, 1930

LOYAL DAVIS, M.D., *President, in the Chair*

A CLINICOPATHOLOGIC STUDY OF THE INTRACRANIAL ARACHNOID MEMBRANE. LOYAL DAVIS and HALE HAVEN (by invitation).

Ten cases that showed definite histopathologic changes in the arachnoid membrane were presented. Specimens of the arachnoid membrane removed in cases in which, at the time of operation, the surgeon thought that he was dealing with a form of circumscribed arachnoiditis were studied. These included one verified case of intracranial tumor, two with the pathologic process centering about the optic chiasm and seven with the clinical picture of an intracranial neoplasm in which no tumor was verified at operation. Each of the cases showed definite changes in the arachnoid membrane, which the authors were able to classify into three different groups: (*a*) inflammatory, (*b*) fibrous and (*c*) hyperplastic, according to the histopathologic picture presented.

Two of the patients gave a history of trauma sufficient to be considered as an etiologic factor. No attempt was made to discuss the etiology in the other cases. There was an uneventful postoperative recovery in every case. All of the patients obtained some measure of relief from their symptoms. When the pathology was located in the posterior fossa or about the optic chiasm, there was a more complete recovery than when it was found over the convexity of the hemispheres.

DISCUSSION

DR. G. B. HASSIN: Would it be permissible to diagnose the condition as external hydrocephalus in the case in which an exudate was found after opening the arachnoid? In external hydrocephalus there is usually hydrops of the brain itself, which may produce all the signs and symptoms of a tumor of the brain.

DR. HALE HAVEN: The pathologic process of the brain in the case to which Dr. Hassin referred was not studied. There did not appear to be marked cerebral adhesions in the region in which the hemisphere was observed. The strands of the arachnoid under the pia were not thickened, nor were they markedly increased in number. If one considers external hydrocephalus, there was not a marked increase in the size or filling with fluid, nor were the fibers thickened. Those about the chiasm were of the thick nature of which, I believe, Dr. Hassin is speaking.

GENUINE EPILEPSY: STUDIES OF THE MICROSCOPIC CHANGES IN THE CAPILLARY SYSTEM AS A PROBABLE ETIOLOGIC FACTOR. DR. D. M. OLKON.

This paper was published in full in the *Journal of Nervous and Mental Disease* **72**:538 (Nov.) 1930.

DISCUSSION

DR. H. I. DAVIS: What is the frequency of epilepsy per one thousand or one hundred thousand of the population, and how does this compare with apparent injury at birth?

DR. MEYER SOLOMON: I recall seeing a report of some experimental work within the last few years, in which the authors showed from observation of the human cortex during a convulsive state that an anemic state existed; the cortex became very white with the tonic phase of the convulsion, and then became reddened during the clonic phase. Can Dr. Olkon correlate any of his experi-

mental work with this, and has he observed anything like this in experimental animals?

Dr. Olkon mentioned several times that the metabolic changes are produced as a consequence of the cerebral changes. How can the general metabolic changes be produced by small vasomotor disturbances in the cortex?

DR. G. B. HASSIN: Does the brain pulsate in the attacks or does it not?

DR. JOHN FAVIL: Will Dr. Olkon explain more fully how the capillary hemorrhagic state, resulting in metabolic changes which may account for convulsive phenomena, can be delayed for so many years in the production of convulsions, as frequently is the case. Convulsions often do not appear until a patient is 10, 15 or 20 years of age.

DR. D. M. OLKON: Is it not permissible to assume that if an organism had no tendency toward a derangement of the central nervous system, it would resist the advent of the convulsive state on the basis that fewer persons are afflicted with "idiopathic" epilepsy? Birth trauma, although producing some injurious effects in many of the new-born, does not always produce this particular epileptic state. On the other hand, persons with a more labile central nervous system tend to react to birth traumas in this way by the nutritional interferences caused by the capillary imbalance produced at that time, which is one phase of susceptibility. Nothwithstanding the assumption of susceptibility, there has to be something that will initiate and set up an effect. This particular effect is set up by injury to the capillaries, and the subsequent nutritional interferences caused by it help to form the vicious circle, giving rise to the phenomenon of idiopathic epilepsy.

Regarding vasomotor disturbances, Dr. Solomon may recall the slides on which were shown the responsive changes in the capillary network. For example, in one of the slides it was clearly demonstrated that in the experimental animal after a rigor, the brain capillaries as well as the surface capillaries showed stasis at the arch and rupture at points of bifurcation as well as ischemia in the distal portion; the portion between the arch and the distal portion was also dilated, showing capillary atony. All of these changes were microscopic observations.

In answer to the question whether the brain pulsates during a convulsion, I may say that in the dog, immediately following a convulsion, the microscopic vessels are seen to pulsate intermittently pari passu with the active spasm of the capillaries and the subpapillary plexuses.

DR. G. B. HASSIN: The whole brain?

DR. D. M. OLKON: No, I have not observed that.

I did not attempt to discuss the rôle of biochemistry in the process of capillary changes. I confined my paper to the observed physical changes of the capillaries. The second point made by Dr. Favill, that the time interval between the birth trauma and the subsequent convulsive state in many instances is quite long, can be explained as a delayed conditioned response. Moreover, there are in many instances early signs in epileptic persons, in the form of tics, muscular unrest, spastic constipation and vasomotor changes, indicating an unstable central nervous system as well as an autonomic system. The body naturally tends toward metabolic equilibrium, but finally breaks down when the central nervous system, constitutionally, is no longer able to compensate for the injury originally incurred at birth. Of course, birth trauma initiates many other changes; too many, indeed, to be mentioned here. My attention was centered particularly on the capillary changes, and in this capillary disturbance, I believe, the probable etiologic factor in the group of persons suffering from so-called idiopathic epilepsy may be found.

PARAPLEGIA IN HODGKIN'S DISEASE. PHILIP SHAPIRO (by invitation).

This paper appeared in full in the ARCHIVES (**24**:509 [Sept.] 1930).

DISCUSSION

DR. G. B. HASSIN: I saw one specimen from Dr. Shapiro's case in which the granuloma was situated outside the dura; at this level there were marked

changes in the spinal cord. Grossly, they were analogous to those seen in subacute combined degeneration of the cord. Microscopically, however, there were some differences. The main difference was that in subacute combined degeneration, the changes are scattered throughout the cord, whereas in this case they were confined to a limited area. Above and below the latter, there were practically no changes. The gray matter was not involved in the sections that I saw. It would probably be premature to identify the microscopic changes described by Dr. Shapiro with those seen in subacute combined cord degeneration. For this, further work on a larger amount of material is necessary.

DR. ARTHUR WEIL: The present discussion reminds me of a similar one at a meeting of the New York Neurological Society (Blakeslee, G. A.: Spinal Cord Compression in Hodgkin's Disease, ARCH. NEUROL. & PSYCHIAT. **20**:216 [July] 1928) on the occasion of Blakeslee's paper on the treatment of spinal cord invasion in Hodgkin's disease with roentgen rays. He shared the opinion of many other clinicians that the lesions of the spinal cord in this disease are of a local nature, i. e., produced either by pressure of the granulomas invading the spinal canal or by focal disturbances of the blood and the lymphatic circulation. He did not share Globus' opinion that a systemic degenerative disease was the underlying pathologic condition of the clinical picture of paraplegia. Davison and I studied changes in the spinal cord in Hodgkin's disease in six cases of our own and reviewed those published in the literature. It seemed to us that the secondary anemia that appears in the later course of the disease, as in other cachexias following malignant tumors, could not be responsible for the changes in the spinal cord which were reported. Such changes could be traced either to invasion of the spinal canal or of the intervertebral foramina by the lymphogranulomas with the sequelae of myelomalacia following pressure and interference with blood and lymphatic circulation. In one case of extensive retroperitoneal Hodgkin's disease, a bilateral degeneration of the pyramidal tract was found, but subacute combined degeneration of the spinal cord was not observed.

As to Dr. Shapiro's first case it seems to me that, judging from the lantern slides, one is dealing with a localized myelomalacia of a segment of the lower spinal cord, which clinically produced the syndrome of a complete transverse lesion of the spinal cord with a rather rapid course. The statement that tumor masses were found at this level gives a ready explanation for the degenerative changes. But one cannot call this localized transverse myelomalacia a subacute combined degeneration. Dr. Hassin himself described this condition, which is not, as it was stated in the older literature, a combined funicular myelitis, but which starts in isolated foci of destruction of the white matter of the spinal cord. The intense damage of the glia prevents its reparative reaction and the "Lueckenfelder" remain. The interruption of the nerve fibers produces ascending and descending secondary degenerations, and by the enlargement and confluence of the primary foci in combination with these secondary degenerations the typical picture of subacute combined degeneration is produced. Pernicious anemia is the classical representative of this disease. As to Dr. Shapiro's second case, one must regret that he did not show lantern slides or microscopic preparations, which would have given a better conception of the pathologic changes. Judging from his description of the degeneration of the posterior columns and of the outer parts of the posterior lateral columns, which he found in the upper part of the spinal cord, bilaterally, one is under the impression that he described the picture of the early stages of an ascending degeneration of the long fiber tracts following a complete transverse lesion of the spinal cord at a lower segment. Before one assumes the effect of a hypothetical toxin produced by the lymphogranulomas, one should consider other local possibilities. Could Dr. Shapiro rule out the possibility that the posterior roots of the dorsal and lumbar segments of the spinal cord were invaded by the mediastinal and retroperitoneal masses of which he spoke? Is he sure that no focus of a transverse myelomalacia in the lower dorsal segments existed, which might have been produced by an epidural invasion of the granulomas with thrombotic or embolic vascular lesions?

DR. ROY GRINKER: It is always interesting to hear doubtful conditions ascribed to yet more doubtful physiologic phenomena. I think that Dr. Shapiro in interpreting his first case must prove, or show that it has been proved, that such processes as obstruction in the perineural or subarachnoid space have led to the particular lesion described. I have never been convinced by physiologic experiments that the spinal fluid obtains its main portal of exit through the perineural sheaths. All evidence, I think, shows that the spinal perineural spaces form the least important means of spinal fluid circulation. I cannot conceive the obstruction of one or two spaces causing the change in spinal fluid pressure up and down within the cord, nor can I conceive of the tissue juices not making use of spaces about other roots. I do not think it is possible in this case of myelomalacia to adopt as an explanation a hypothesis that has not been proved. I, too, think that a thrombosis at that level has possibly been overlooked.

DR. PHILIP SHAPIRO: In the first case I tried to emphasize that there was no pressure whatever on the underlying cord. Whatever produced the myelomalacia, it was not produced by pressure, nor was it produced by thrombosis, for we studied numerous sections and discovered no thrombosis. I can offer Dr. Grinker no explanation for this morphologic change. All I can say is that the changes corresponded exactly to the level of the changes in the arachnoid.

Dr. Hassin saw the slides in the second case and also in the case of the granuloma of the prostate gland, and there was no question but that they showed the picture of subacute combined degeneration. I am sure that Dr. Weil, if he saw them, would agree with this.

SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD WITH CHRONIC CHANGES IN THE ANTERIOR HORNS OF THE CERVICODORSAL REGION: A HISTOPATHOLOGIC STUDY. THEODORE T. STONE.

In the case here reported, the diagnosis from a clinical standpoint was subacute combined degeneration of the spinal cord. In addition, there was clinical evidence of wasting of the small muscles of the hand; in explanation of this, cellular changes — axonal reaction in the anterior horns of the cervicodorsal regions — were found. The question arises as to the relation of the wasting of the muscles of the hand and changes in the anterior horns of the cervicodorsal region and the degeneration of the posterior lateral columns. There was found a definite involvement of the anterior roots in the cervicodorsal region. The anterior root fibers could not be traced from the roots to the anterior horns in the white matter of the anterolateral columns. A retrograde anterior horn cell change could result from this radicular neuritis.

DISCUSSION

DR. G. B. HASSIN: Did the changes in the anterior horns show any clinical manifestations such as muscular weakness, electrical changes of the nerves or atrophies?

DR. GEORGE W. HALL: I think that Dr. Stone's diagnosis is certainly within the limits of possibility, because of the fact that there is so frequently an involvement of the peripheral nerves in cases of combined degeneration of the cord. There may be definite changes in the central nervous system, even though the blood picture is absent. The absence of free hydrochloric acid in the stomach is one of the important things. The question occurred to me, in connection with Dr. Shapiro's case, whether free hydrochloric acid had been found in his patient. At St. Luke's Hospital a patient was seen not long ago who had recovered from neuritis, absent knee jerks, pain on pressure over the calf muscles, weakened extensors, etc., but still had an absence of free hydrochloric acid in the stomach and a modified blood picture. Another patient had definite bilateral foot-drop, marked tenderness over the calf muscles, severe paralysis, as well as the typical blood picture and absence of free hydrochloric acid.

DR. ARTHUR WEIL: The last remark of Dr. Hall's is well illustrated by publications of the last years regarding cases of pernicious anemia which revealed

themselves neurologically only as peripheral neuritis and which at autopsy showed no marked changes of the spinal cord. In Dr. Stone's case I think that the evidence of a primary peripheral lesion with retrograde degeneration of the anterior horn cells is suggestive.

DR. ROY GRINKER: The peripheral neuritis and changes secondary to it in pernicious anemia have been well worked out by Hamilton and Nixon. They found that peripheral changes in the nerves could be demonstrated clinically and at necropsy. It is interesting how frequently one observed these changes in pernicious anemia, and I think it may be stated that it is these changes that improve under liver therapy, rather than the symptoms referable to pathology in the central nervous system. Furthermore, as I have previously stated, it is these peripheral nerve changes which have led Woltman, among others, to state that 80 per cent of cases of pernicious anemia are associated with signs of combined cord degeneration. The correct figure of true central changes, probably irreparable, is about 30 per cent.

DR. THEODORE T. STONE: In answer to Dr. Hassin, this case from a clinical point of view was poorly worked up. The patient was seen outside the hospital by Dr. William H. Holmes, who said that he found definite atrophy of the small muscles of the hand. According to the history obtained, the onset of the condition was characterized by paresthetic sensations in all four extremities. The history was not complete. We had only three or four pieces of the cord, and not until the examination was made was there any question about changes in the anterior horn cells.

Dr. Weil's remarks about peripheral neuritis are appreciated, for in this case there was no observation that would justify any other conclusion.

I wish to thank Dr. Hassin for his help in this case. Dr. Woltman saw these slides and thought that in all probability the changes were the result of neuritis.

Regular Meeting, Oct. 16, 1930

A. B. YUDELSON, M.D., *Vice-President, Presiding*

SOME EXPERIENCES WITH "JAKE" PARALYSIS. DR. ROY R. GRINKER.

On July 27, 1930, by permission of the department of health, with Dr. Sigfrid Maurer, I examined seven patients with "jake" paralysis in Villa Grove, a small community in southern Illinois. The town centers around a junction of a railroad, and most of the inhabitants make a living either directly or indirectly through the railroad.

CASE 1.—O. A., aged 41, an American, a railroad switchman, who had been in excellent health the previous winter, drank the contents of one 2 ounce bottle of "jake" about April 15. Three days later, he felt badly, but worked through the entire month. In the latter part of April and during May, he complained of soreness in the muscles of the calves as if he had worked in the garden too long. On June 2, he could not walk because of severe pain in the calves and bilateral foot drop which developed suddenly. The cramps persisted through the month of June and into July, when the trouble was most marked and he was unable to get out of bed without assistance. He had, however, been improving during the last week of July. His complaint at the time of examination was lack of balance, but he could walk when supported. At first the feet were swollen, but later the swelling was present only when he stood for some time.

Examination revealed no power in the toes or muscles of the feet. The ankles were immobile and there was bilateral foot drop. Only a slight plantar arch was present. There was fair flexion and good extension of both legs, good flexion

and extension of the thighs, some flabbiness of the muscles of the calves and thighs, but no visible atrophy. The fingers of the right hand could not be abducted, adducted or extended. There was a characteristic position of the fingers: extension at the metacarpophalangeal and slight flexion at the second phalangeal joints. There was slight ability to flex the fingers of the right hand. Flexion and extension of the right wrist was very weak. In the left hand there was better flexion in the fingers, and extension could be made more complete. There was no abduction or adduction of the fingers. There was marked atrophy of the muscles of the left forearm and of the small muscles of both hands. The achilles jerks were absent, the knee jerks bilaterally lively. The abdominal reflexes were present, and all the deep reflexes were equal and lively. The cranial nerves were normal. There was no change of tactile or vibratory sensibility but there was a definite distal hyperalgesia of the hands and feet.

CASE 2.—E. P., aged 51, a fireman and engineer, had been in good general health except for rheumatism in 1917. He was "not much of a drinker" but admitted that he had tasted "jake." He was not convinced that the "jake" brought about the present condition (because he would lose his job with the railroad). The first indication of the trouble was numbness of two fingers. After about two weeks, on April 15, soreness developed in the calves of the legs as if he had been jumping. At first he was unable to move the hands or feet, and there were twitchings in the muscles over the lower part of the spine and hips and sometimes in the toes.

Physical examination revealed that both feet were edematous. No motion of the toes was possible, and no flexion or extension of either ankle. The right leg could be completely extended but not flexed. The left leg could be extended slightly better than the right. Flexion and extension of both thighs was very weak. There was definite atrophy of the muscles of the feet and the anterior and posterior muscles of the thighs, and some atrophy of the muscles of the calf. There was marked atrophy of all the muscles of the hands with a claw position. A slight flexion of the distal phalanges in the fingers was possible but not extension. There was slight adduction of the thumb. Flexion of the forearms was somewhat weak, but extension was good. There was no power in the flexors of the wrists and very little in the extensors. The achilles jerks were absent on both sides though an adductor response of the thighs resulted. The knee jerks were lively, the superficial reflexes normal, and the Babinski reflex negative. The upper deep reflexes were all equal and lively. All forms of sensation were normally perceived.

CASE 3.—J. W. H., aged 50, a shoe repairer, who had always been in good health, during the past year had taken on an average a fourth of a 2 ounce bottle of "jake" daily. "Probably once in a great while" he would drink some whisky, but very little. He believed that the batch of "jake" that caused his difficulty was different from others he had taken in both taste and effect, because after drinking three fourths of a bottle severe diarrhea developed, which lasted a week and was followed by obstinate constipation. G. B. and H. (cases 4 and 5, respectively) drank with him at that time and both developed paralysis, while two others who drank of the same batch did not become sick. He felt sure that dozens of people in the town had drunk this same liquor and expressed surprise that only a few developed paralysis. Incidentally, this man was the go-between for a bootlegger who disposed of "jake" in this town.

On the afternoon of April 16, pains developed in the calves of the legs, which he thought was due to working in the garden. That afternoon he became chilled because of a change in the weather, and by evening he noticed that there was bilateral foot drop on walking. The following week he worked hard all day in the shop, and during the latter part of the day it became difficult for him to pick up tacks with the thumb and forefingers. The calves were sore and slightly swollen. He had had no sharp pains at any time but simply a soreness along the tendons. He denied any loss of sensation. The hands and legs were badly swollen at first but not later.

Examination showed marked atrophy of the muscles of the feet and of the anterior and posterior muscles of the calf and thigh of both legs. The only movement possible was a slight extension and extremely minute flexion of both legs. There was a slight flexion and extension of the fingers and good flexion and extension of the wrists, better, however, on the left. There was marked distal atrophy of the forearms. The achilles reflexes were absent, and the knee and upper deep reflexes markedly exaggerated. The muscles of the trunk were normal. The only sensory change was a distal hyperalgesia in the feet and hands.

CASE 4.—G. B., aged 73, a retired farmer, had been a habitual drunkard for eleven years. Before Palm Sunday he had been drinking home brew. He drank "jake" in February without ill effects. The last drink of "jake" was on April 12, on the persuasion of J. W. H. (case 3), at about 3 p. m. The next day (Palm Sunday) it was hard to raise the feet, but he went to church. On Monday he was no better, the muscles in both calves being sore, and when he awoke on Wednesday he could only crawl on hands and knees. A friend, W. R., was immediately consulted because he had had three drinks of "jake" with the patient, but he had been completely normal. There had been some improvement in the patient's feet, in that at first he had no feeling whatever in the extremities and there was now some sensation.

Examination showed marked edema of the feet and ankles, definite atrophy of the small muscles of the feet and absence of the plantar arch. He could not move the toes or feet in any direction. There was slight flexion of the left leg and extremely weak extension. The right leg, if anything, was worse. The muscles of both calves were definitely atrophic, and the muscles of the thighs were profoundly wasted. There was very weak flexion of the thighs and only fair strength in extension. The achilles jerks were absent but the knee jerks were equal and lively. The abdominal reflexes were present. There was marked atrophy of the small muscles of the hands. The forearms, especially the right, were also atrophic. Abduction, adduction and flexion of the fingers and toes were impossible, but the extensors had fairly good strength. Extension was good in both wrists, but flexion extremely poorly performed. Movements about the elbow joints were normal. The upper deep reflexes were normal. Tactile and vibratory sensation was definitely decreased in a stocking area below the knee. Pain sensibility was normal.

CASE 5.—H., aged 57, a stockman, who had been in good general health and had lost no time from work in twelve years, had been drinking "jake" occasionally for six or seven months. The last drink was taken with J. W. H. (case 3) and E. H. (case 6). About seventeen days after this drink of "jake" he was unable to go to work because of aching calves. Six or eight days later, foot drop developed. Two weeks after the onset, the wrists began to drop. At first there was marked swelling of both feet, but this had practically subsided. Instead, there was swelling in both hands. He occasionally had some twitchings of the muscles of the toes. There had been no subjective sensory changes. No movement of the feet or toes was possible, and flexion of the legs was very weak, while extension was slightly better. The flexors of the trunk were extremely weak as were also the flexors and extensors of the thighs. There was marked atrophy of the anterior muscles of the thighs but only slight wasting of the muscles of the calves. The achilles jerks were absent on both sides with markedly exaggerated knee jerks. There was a distal hyperalgesia, but normal tactile sensation. There was marked atrophy of the muscles of the hands and forearms on which was superimposed edema. Flexion of the forearms was moderately weakened. There was complete wrist drop, but slight flexion of both wrists was possible. The wrist jerks were decreased, but there were normal biceps and triceps reflexes. There had been decided improvement in the last ten days. He could feed himself and raise up from an arm chair and walk behind a chair.

CASE 6.—E. H., aged 59, a shop fireman, who had had heart trouble for years, had not been a drinking man, but while in J. W. H.'s (case 3) store was

offered a drink of "jake" because he came to pay his bill, and took a small swallow. Three weeks later, he noticed aching in the calves of the legs and swelling of the feet. The heart pounded considerably and he thought that he was suffering from heart trouble, but he soon realized that he had the same trouble as the other affected townsmen. No movement of the toes of the right foot was possible. There was marked weakness in flexion and extension of the right foot but stronger flexion and extension in the left foot, and moderate atrophy of the muscles of both calves. Both ankle jerks was absent, and the knee jerks were exaggerated. There was no sensory loss, and no change in the trunk or upper extremities.

CASE 7.—W. B. H., aged 37, a fireman, who considered himself a drinking man, prior to the present illness had been drinking home brew. His first drink of "jake" was taken in February; the second drink, of two 2 ounce bottles, was taken on Easter Sunday, April 20. Two weeks later, he felt pain in the calves of the legs. He continued to work and drink home brew; in fact, he said that it made him feel better. The sensation in the calves was as if he had been "standing on a ladder all day." The soreness persisted, and he felt that the feet had become flat. The next day foot drop developed and there was a tingling sensation as if the feet were asleep. Because others who had been drinking "jake" had been affected for two weeks, he realized that he had the same trouble.

He had had some twitchings in the legs, but never in the hands.

Examination showed bilateral foot drop, more marked in the left, with atrophy of all the small muscles of the feet. There was moderately good tone of the muscles of the right calf but the left was atrophic, especially the posterior group. The muscles of the thighs were atrophied as well. There were no movement of the toes, no power in plantar or dorsal flexion of the ankles, very weak flexion of the left leg with much better extension, and fair flexion of the right leg with normal extension. Flexion in both thighs was weak, there being good extension. Occasional coarse fibrillations of the muscles of the thighs were seen after voluntary movement. The achilles reflexes were absent, the knee jerks exaggerated, and the plantar responses normal. The abdominal reflexes were absent, although the cremasteric reflexes were equal and normal. The hands were held in a characteristic position, in which the thumb was flexed with the metacarpophalangeal joint extended and on a line with the palm. He had a typical claw hand. There was marked atrophy of the small muscles of the hands, especially of the first interossei and the thenar eminences. No abduction or adduction of the fingers was possible. Flexion and extension of the fingers was practically impossible. The thumbs were immobile. The wrists could be only feebly extended and weakly flexed. Flexion and extension of the forearms was weak, and flattening of the muscles of the anterior surface of the forearms was noted. There was no disturbance of the muscles of the upper part of the arms or trunk. Sensation was intact in all modalities. The upper deep reflexes were lively.

Comment.—The seven persons reported on and probably many others in this small town had been drinking "jake" for some time; J. W. H. (case 3) had been selling and drinking it all the year. It was evident to him that the recent batch was different; a few weeks later, he realized with the onset of the paralysis that it really was different. Not all who drank from this batch suffered from paralysis. Some of those who were affected were chronic drinkers and called themselves "drinking men." Others could not be called hard drinkers. The previous history, the type of occupation and the mode of living seemed to have nothing to do with the development of the paralysis. There was no febrile reaction suggestive of the onset of an infection; nor did trauma play any rôle. The time of onset after drinking was variable, usually being from two or three weeks, although in one case paralysis occurred within two or three days. The amount of "jake" necessary to produce the paralysis also varied, the minimum amount being apparently one swallow, although the reliability of the testimony in this regard may be doubted.

The parts affected were distal in both the lower and the upper extremities. The small muscles of the hands and feet were predominantly affected with atrophy,

paralysis and loss of reflexes. The proximal involvement of the extremities was variable but in all cases was associated with little atrophy and with exaggerated reflexes. The patients stated that fibrillations were occasionally present, and examination revealed them in one case. The sensory changes were those of a stocking and glove hyperalgesia and in one instance hypesthesia. The bladder and rectal sphincters were never involved. A curious dependent edema in the first few weeks was observed by practically all patients. During a period of six months the patients have improved very slightly. One or two have noticed a definite change in sensation and ability to get around, but the majority have remained in the same condition.

From the neurologic observations it would be surmised that the majority of the symptoms are due to involvement of the peripheral nerves, but considerable evidence is present that the whole neuron, including the anterior horn cell, is affected by the poison. It seems from a study of these cases that the paralysis is due to something present in the sample of Jamaica ginger used, which was not a usual ingredient of that beverage.

DISCUSSION

DR. A. B. YUDELSON: Were there any electrical changes and was direct myotatic irritability of the muscles involved?

DR. ROY R. GRINKER: There was no increase in myotatic irritability, although all patients were tested. The electrical reactions were not tested.

The surprising increase in reflexes in the quadriceps muscles in the presence of atrophy is worthy of reiteration. Never were any of the upper reflexes absent, whereas the achilles jerks were gone in all cases.

Dr. Singer asked me whether we had examined the hair for arsenic. This was not done because of the small amounts of Jamaica ginger these persons had consumed. We made a sort of ethical examination of all these men and found the shoemaker the least reliable. The man who said he took the least amount of the mixture and had the least involvement of the muscles was the most worthy of trust.

A CASE OF AN AGRAMMATICAL SPEECH DISTURBANCE IN THE ENGLISH LANGUAGE. DR. A. A. LOW.

This article appears in this issue, p. 556.

ELEVENTH ANNUAL INTERNATIONAL NEUROLOGIC ASSEMBLY

Paris, June 3-4, 1930

DRS. A. WINKLER, DE BEDO, J. PURVES-STEWART AND FEDELE NEGRO, *in the Chair*

THE NEUROGLIA AND ITS PATHOLOGIC REACTIONS. G. ROUSSY, J. LHERMITTE and C. OBERLING.

The neuroglia, first described in 1846 by Virchow as the connective tissue of the nervous system, was subjected to studies by Ranvier and Weigert, who came to very different conclusions as to its nature, and later by Held, and especially by Golgi and Cajal who by their selective impregnation methods revealed many of the characteristics of this common type of tissue. The work of Robertson in 1897, differentiating the mesoglia, was followed in 1913 by Cajal, and later by del Rio-Hortega, in the illumination of this most important cell. Finally,

the oligodendroglia was separated by the last-mentioned author from the microglia. The studies of Nageotte on the cell of Schwann brought into harmony the conception of a peripheral neuroglia of importance, both nutritive and supportive.

The authors limit themselves to the consideration of the neuroglia proper.

The macroglia is found in two forms: protoplasmic and fibrillary astrocytes (also known as spider cells and Deiters' corpuscles). The protoplasmic type is recognized by its vesicular nucleus, a moderate amount of cytoplasm and abundant tortuous processes of irregular caliber. The fibrillary astrocytes, on the other hand, have special processes brought out by selective stains which are delicate, swing past the body of the cell with apparent little connection with it, do not branch and are not particularly wavy. They seem to have no anastomoses. One or more of these processes, usually heavier, connects with the perivascular sheath of the blood vessel by means of a terminal expansion or foot. The protoplasmic astrocytes are found particularly in the gray matter, the fibrillary in the white matter. A much debated question has been the relation of the neuroglia fibrils to the cells. It seems now that these fibrils are formed by the astrocytes but, analogous to white fibrous connective tissue, are not always connected with the cells.

The oligodendroglia consists of small, round, rather dense nuclei; in successful impregnations a moderate number of rather tortuous branching processes of a very delicate character can be seen running out in all directions. The perinuclear cytoplasm is very slight. These cells have no connection with the blood vessels; they are found both in the gray matter, where they make up the majority of satellite cells, and in the white matter, where they comprise the interfascicular glia, and they are found at all levels of the nervous system. The following types are distinguished: those found in the white matter; those sending a few rather large projections out between the bundles of nerve fibers, and those resembling the cells of Schwann, the prolongations of which are frequently encountered as helices about large nerve fibers. It would seem that, in the peripheral nerve, cells greatly resembling the oligodendroglia send a process about the cylinder axis at nodal points.

The microglia consists of a small round or elongated nucleus and the cytoplasm, which is often fusiform and contains a number of granules. Gliosomes are not found in this type of cell. These cells are found throughout the nervous system, especially about the nerve cells and the smaller blood vessels. Their processes never become attached to the wall of a vessel. The morphology of this cell varies greatly, not only with the location in the brain but also with the location in the cortex.

The glia fibrils which are the product of the macroglia are considered now to form a syncytial reticulum, in spite of the data indicated by impregnation methods which show each cell distinct. The syncytium due to the cell of Schwann is generally accepted. The glia fibrils are particularly important at the boundaries of the nervous system, both within and without, and along the blood vessels.

A study of the perivascular space recently by Schaltenbrand and Bailey has thrown much light on this question, particularly the fact that this membrane is traversed with difficulty by cells. The space of His, supposed to be between this pia-glia and the nervous system proper, is considered an artefact.

In passing out of the central nervous system the nerve fibers become changed at this boundary, lose their accompanying neuroglia of central type and take on the character of peripheral nerves.

The glia is developed from the lining cells of the neural tube through progressive differentiation. It would seem that the medulloblasts are undifferentiated cells capable of developing into either neuroblasts or glioblasts. The astrocytes and the oligodendrocytes would seem to develop from the same cell; but the origin of the microglia is much discussed, del Rio-Hortega, Marinesco and others believing in its mesodermal origin while the authors believe it to be of ectodermal derivation.

The function of the neuroglia as a supporting tissue is generally accepted. Its nutritive rôle is accepted by many.

The direct connection between the vessel and the nerve cell being accomplished by the processes of individual astrocytes, some believe that the neuroglia cells possess a secretory function, in the sense of a power of elaboration, which is indicated by an alteration in the myelin; a few believe that the neuroglia has an interstitial secretory function, while Cajal believes that by the contraction and expansion of the processes communications may be established between neurons, but this, as well as its insulating function, the authors consider hypothetic.

THE PATHOLOGIC REACTIONS OF THE NEUROGLIA

There is scarcely a lesion of the nervous system in which the neuroglia plays no part, and in most of them the neuroglial reactions give to the lesions their characteristic appearance. The form is extremely variable on account of the great structural differentiation of the elements, their plasticity and the manifold etiologic factors. The various types of neuroglia cells possess very different sensibility in regard to the same pathogenic agent, and they present peculiarities of reaction which are unique. Thus one may see in similar lesions both degenerative and proliferative phenomena, and each of these may present different appearances in different types of neuroglia cells. Moreover, the mesodermal tissue often takes part in the reaction and gives rise to various infiltrating cells.

Neuroglia cells may degenerate or even die. They metamorphose, lose their processes, become mobilized and even multiply. In the beginning, the degenerative phenomena are of primary importance. In the second stage, there is characteristic mobilization, phagocytosis and absorption of the products of disintegration. In the third period, multiplication appears with the formation of the cicatrix. Moreover, the fibrils go through similar processes: first, degeneration, and later, proliferation, giving rise to sclerosis. However, there is practically always a mixture of degenerative and proliferative phenomena. Sometimes the proliferative precedes the degenerative, as in the case of syringomyelia and tumors.

1. *Disintegrative Processes.*—During degeneration, the nuclei of the glia cells become smaller and hyperchromatic, often with irregular contours, sometimes fragmented. In acute processes, however, the nucleus is swollen, the chromatin scattered, and sometimes the nucleus appears vacuolized and contains small droplets of fat. Karyorrhexis and karyolysis terminate the degeneration. The cytoplasm may be either contracted or swollen, the processes correspondingly visible or broken up. Fatty substances are common in the cytoplasm.

One of the characteristic acute degenerative lesions of the astrocytes is ameboid transformation. The cytoplasm becomes swollen; the dendrites are lost; the nucleus, at first hyperchromatic, becomes degenerated, and the cytoplasm, more visible than normal, becomes cystic and encloses lipoid and basophilic corpuscles. At a more advanced stage, the dendrites, which are broken off, likewise become filled with basophilic particles. The ameboid cell was thought by Alzheimer to be a reactive change, but it is now thought to be due to degeneration. There is a possibility that it may even result from postmortem changes, but the authors compare this to the similarly obscure problem of fragmentation in the myocardial fibers, the exact significance of which is not known. When degeneration is slower, the astrocytes take on extremely variable features. The cytoplasm is enlarged, the processes show irregular swellings and varicosities and become fragmented, and the débris is phagocytized. This procedure is often accompanied by the formation of new processes. These much enlarged cells, the cytoplasm of which may contain fatty globules and even multiple nuclei, often exhibit a few long processes; they were described by Nissl as the gemästete Gliazellen. Degeneration thus reduces the astrocytes to more simple forms. Such have been encountered in the experimental lesions produced by the authors in applying radium to the cerebral cortex. At times monster cells are produced. In these degenerative lesions certain astrocytes may be seen, the bodies of which are infiltrated by fatty materials. In the terminal stages these may become detached from vessels and turned into true granular corpuscles.

The oligodendroglia is the most fragile of the cells and becomes rapidly altered post mortem. In many conditions the cells become acutely swollen; the cytoplasm is granular and the nucleus pale. In the second stage, the cytoplasm increases irregularly in volume and the nucleus becomes hyperchromatic. More severe stages are recognized by a fragmentation of the processes, and finally the swelling of the cytoplasm becomes extreme, the body is filled with vacuoles and the cell disintegrates. The nucleus, which is first swollen, later becomes pyknotic. Not infrequently these cells also become filled with fat granules, and they eventually play a part in the elaboration of compound granular corpuscles. This observation, however, is debated. The cytoplasm of the oligodendroglia may be the site of a peculiar transformation in which mucoid material appears. This indicates a severe transformation which is probably irreversible. The mucoid material probably hampers the activity of the cells and leads rapidly to death. The oligodendroglia cell can also undergo atrophy with the production of starlike nuclei. The oligodendroglia is apt to show somewhat the same transformation as the microglia and the macroglia, but it is the most sensitive element of the nervous system and the most likely to react.

2. *Phenomena of Mobilization and Phagocytosis.*—The origin of the compound granular corpuscles has recently been called into question by del Rio-Hortega and his school. The authors contend, however, that all the elements of the neuroglia participate in the formation of these cells. They appear in conditions of destruction of the ganglion cells, in degenerative conditions affecting the nerve fibers and in more complex degenerative conditions such as softenings. Ganglion cells undergoing degeneration are surrounded by satellites which, if the condition is severe, become round and phagocytize the disintegrated protoplasm. These products are transported to the perivascular spaces. The satellite cells live in symbiosis with the ganglion cells, in the same manner in which, at the periphery, the fibers and cells of Schwann exist. When the nerve cells degenerate, the satellites proliferate. These satellite cells are both microglia and oligodendroglia.

Only in cases in which the cell dies and disintegrates is there any actual phagocytosis, and these cells are not to be looked on as in any way harmful to the live elements. In secondary degenerations the microglia and oligodendroglia proliferate two or three hours after the injury; they take on migratory and phagocytic qualities. The first have been called myeloclasts, and belong to the microglia. These penetrate the myelin sheaths, envelop the axis-cylinder, take up lipoid granules and become granular corpuscles. These cells are of the same morphology as those which are described as myeloplasts, the function of which is the construction of nerve fibers. Later, the myelophages are derived from the microglia and oligodendroglia, and these are often united in a syncytium but are sometimes isolated. They also become phagocytic and appear as fat granule cells. Finally, the third variety of fat-bearing phagocytes is derived from the macroglia. All these cells undergo fatty transformation, the protoplasm is destroyed, the membranes finally rupture and the nucleus shrinks and breaks up. The products of disintegration set free in this neuroglia reticulum are taken up by other elements, finally passing the pia-glia membrane into the Virchow-Robin space, where they become absorbed by histiocytes.

In foci of softening three types of cells give rise to fat-bearing granule cells: hematogenic, histiogenic and gliogenic. At the beginning, the vascular reactions dominate the picture. Surrounding the necrotic cerebral tissue, the blood vessels are congested and allow passage of leukocytes which invade the necrotic tissue and take up the products of disintegration. The histiocytes from the perivascular sheaths quickly mix with these and soon predominate. Later the reactive phenomena in the neuroglia about the lesion take place, the microglia being first. The cytoplasm enlarges and the processes thicken, shorten and retract. The nucleus becomes irregular and vesicular. The whole cell becomes more globular, with short, thick processes. Phagocytosis begins and the granular corpuscles are formed. During this process the chromatin of the nucleus becomes denser, indicating injury to the cell, and finally the cell ruptures. Most of the granular

corpuscles are formed from the microglia, but the protoplasmic astrocytes can take part in this process, their size and morphology differentiating them from the microglia. In this function the cytoplasm swells, and the processes become thicker; and in the case of fibrillary astrocytes the cytoplasm is dedifferentiated, with dissolution of the fibrils. The body rapidly becomes infiltrated by fat granules, and finally the cytoplasm is represented by delicate trabeculae which run from nucleus to cell membrane. These cells also rupture and disappear. The authors have carried out a number of experiments on the behavior of the astrocytes in the rabbit, producing inflammatory reactions of variable intensity and duration, and from these they draw the following conclusions: In rapidly developing lesions the astrocytes show no tendency to mobilization. Those involved degenerate and disappear, the others persist and enlarge. In more slowly developing lesions, such as those due to irradiation, marked vascular lesions with hemorrhages and necrotic areas are found. Extensive degeneration of the nerve elements, with proliferation of the microglia is found. The astrocytes show variable pictures: Some are frankly degenerative, with swelling of the body, varicosities of the processes and disappearance of the dendrites; others are infiltrated by fatty material, lose their dendrites and turn into round, vacuolated elements the nature of which is still recognizable owing to the persistence of the vascular foot. Finally, these elements become completely detached, show no processes at all and disintegrate. The authors claim that although the microglia is the most active phagocytic cell, the oligodendroglia and, to a less degree, the astrocytes can participate in the function of phagocytosis. The authors see no reason for contrasting the active phagocytosis with the so-called passive infiltration of fatty material in the partly disintegrated cells, since phagocytosis always depends among other things on surface tension of the cell, and this tension is evidently due to a change in the medium in which the cell is located. The conditions are the same for microglia and macroglia, the only difference being that the microglia is better prepared for this function. Recent advances in vital staining have made it possible to study the phagocytic properties of the neuroglia cell from another angle. In the normal animal the normal tissue is never stained because of the neuroglia barrier that prevents the penetration of the dye into the cerebral substance; only perivascular histiocytes are stained. Following intraventricular injections, the epithelium of the ependyma contains fine granules; the dye may penetrate into the cerebral substance; certain astrocytes, and especially the satellite cells, contain fine granules. If the neuroglia barrier becomes more permeable as the result of an inflammatory process, the injured region takes up the dye, which is visible macroscopically. This is especially pronounced in radium lesions treated with trypan blue. The dye is concentrated in the microglia, but is never as intense as in the histiocytes. The authors have noted the presence of vital stains in the interior of the astrocytes. Just recently they observed in embryonal nerve tissue culture of the chick treated with lithium-carmine large cells which might be interpreted as young astrocytes, containing many granules of carmine. These facts indicate that from the standpoint of vital staining there is no absolute difference between the behavior of the histiocytes, microglia and astrocytes; the only difference is in degree. The phenomena of phagocytosis and mobilization of neuroglia gives an insight into the general problem of transportation both of nutritive and of disintegrated elements. In slight degenerative lesions the transportation of these substances is carried on as in normal conditions. The materials flow through the syncytium, traverse the pia-glia membrane, and are taken up by the perivascular phagocytes. If the lesion is more extensive, the glia cells participate in the removal of the débris, the materials being, as it were, passed on from cell to cell up to the perivascular space. The glia barrier being injured and open, the elimination is rapid, but when the barrier closes the process becomes slower. The passage across this barrier is debated, one group of investigators holding that the cells filled with these waste materials can penetrate it, the other that the cells undergo dissolution and that the products of degeneration diffuse through the glia membrane. This opinion is the more likely, since vital stains show that the pia-glia membrane is impermeable, even

to very small colloidal particles. The persistence of products of degeneration outside the barrier is irritating and brings about reaction by the glia with building up of gliosis.

3. *Proliferative Processes.*—Multiplication is a fundamental activity of all the glia cells. It occurs by mitosis or amitosis. On the one hand, there is simplification of the structure of the cell with karyokinesis. On the other, the cell retains its processes and the nucleus divides, the protoplasm separating by fission. Young cells may form fibers or may immediately become phagocytic. Subsequent degeneration is not rare. At a distance from the focus, however, the cells take on adult characteristics. Abnormal glia cells are found in many diseases, such as dementia paralytica, Wilson's disease, pseudosclerosis, neurofibromatosis and tuberous sclerosis, as well as in tumors. The peculiar monster cells in tuberous sclerosis are often difficult to distinguish from abnormal ganglion cells, but transition forms can be found. Giant deformed astrocytes, multinucleated, may be found in Recklinghausen's disease and in the hypertrophic forms of idiocy and epilepsy. Bizarre cells with irregular nuclei described by Alzheimer are found in Wilson's disease and in pseudosclerosis.

Ordinary proliferative processes, however, take place following the destructive focal lesions, and the result is a secondary gliosis. In certain instances, however, the gliosis arises without known cause, but preserves its adult characteristic. The third type of proliferative phenomenon is the tumor glioma.

(*a*) Gliosis: Gliosis appears as the result of any destruction of tissue, following the general biologic rule, although the reason is not clear. Many factors may play a part. The pathogenic agent, in destroying the more sensitive elements, may cause proliferation of the neuroglia which is less sensitive. The processes of disintegration certainly play a part; either direct, by bringing about multiplication of the cells, or indirect, by causing congestion and thus favorable nutritive conditions. Mechanical factors may play a part, and it is known that the increase of pressure up to a certain degree stimulates the multiplication of cells. The last-mentioned phenomenon is probably responsible for the neuroglial proliferation seen near tumors and cysts. The hyperplasia of neuroglia in contact with infiltrating tumors may be explained by the transmission to normal cells of the growth stimulus from tumor cells. The topography and extent of secondary gliosis may be very different. In small foci the gliosis is coextensive with the destruction. On the other hand, if the degeneration is widespread the gliosis will be likewise. The subependymal region and the cortex are the seat of diffuse gliosis, but not always at the location of the primary lesion; thus, in arteriosclerosis the atrophy of the white matter may be accompanied by hypertrophy of the cortical neuroglia. In inflammatory conditions the proliferation of cells is marked, and, although other cells participate to some extent in the gliosis, the astrocytes are dominant. At the border of cicatrizing lesions one finds newly formed blood vessels surrounded by young astrocytes with multiple vascular feet, and later the fibrils develop and pass from one cell to the other. As the process continues, many of these cells drop their fibrils and even disappear, so that the result is a fibrillar tissue with few cells, just as in the formation of scars elsewhere. If the cicatricial gliosis develops in a region where the former histiologic structure is preserved, the new fibers follow the line of the tissue and restore its architecture (isomorphous gliosis). However, if the gliosis develops in a location where no trace of the former tissue persists, it will be irregular, the fibers running in sheaves and bundles in every direction (anisomorphous gliosis). In the formation of cerebral cicatrices the mesodermal elements also play a large part, although this depends on possible injury to the vessels. If the degeneration does not injure the mesodermal barrier, the vessels do not react and little connective tissue proliferation is observed. On the other hand, if the barrier is broken and if the vessels react, the central part of the area is usually made up of a connective tissue scar surrounded by an anisomorphous gliosis. This secondary gliosis may vary extremely in severity, being practically nil in a young person whereas in others it may spread even to the overlying meninges. The experiments of Penfield and Buckley show

that if cerebral tissue is removed with little traumatism there is practically no reaction on the part of the mesenchyma, whereas disintegration of tissue by a blunt needle evokes considerable scar formation.

Primary gliosis is difficult to explain, since no cause is known for the proliferation. It seems to be the primary feature in syringomyelia, tuberous sclerosis and Westphal-Strümpell pseudosclerosis. Oberling has described a meningeal gliosis of congenital origin. Gliosis is sometimes difficult to differentiate from diffuse glioma. Nevertheless, the tumor is much more strictly limited, and is relatively poor in fibrils and richer in cells. The tumor has more blood vessels, and proliferation does not disturb the architecture, but there are many borderline conditions or even combinations.

(*b*) Gliomas: All varieties of neuroglia cells except the microglia can be found in gliomas. Moreover, the behavior of the gliomas is extremely variable and is well correlated with the type of cell. The authors recognize the following types: 1. Astrocytomas, fibrillary and protoplasmic, the cells being large, usually multipolar and with more or less processes. 2. The small cell glioma, probably arising from the oligodendroglia, although in certain instances the nuclei greatly resemble rod cells. 3. The glioblastoma, better known as the "spongioblastoma multiforme," with variable architecture and pseudorosets of degeneration. Rare tumors, such as ganglioneuromas, neurospongiomas and neuro-epitheliomas, are merely mentioned.

Certain secondary phenomena in the proliferative neuroglial tissue deserve mention, particularly hyalinization and liquefaction of the microglia which is seen particularly in vascular tumors, and collagen transformation of the glia fibrils which Nageotte has shown to be laid down between the cells rather than secreted by them. This may be seen in syringomyelia and in ventricular compression, and the collagen is not to be thought of as having a vascular origin. Finally, collagen is found in parts of gliomas devoid of vessels.

Histogenetic, Morphologic, Physiologic and Physiopathologic Concepts of the Microglia. P. del Rio-Hortega.

Historical.—The idea that there are mesodermal elements in the central nervous system is old, but the concept of a mesodermal glia was first sustained by Robertson in 1900. Fifteen years later, Cajal united several different types under the name of the "third element." Del Rio-Hortega finally separated the oligodendroglia from the microglia and demonstrated its sole origin in the mesoderma. "The microglia or mesoglia is of mesodermal (meningeal) origin, possesses greatly ramified, free processes, and is endowed with migratory and macrophagic activities; it is more abundant in the gray than in the white matter, and is found within the general meshwork of nerve and glia fibers as an additional element. On account of its origin and nature, which differ from those of nerve cells (first element) and from those of astrocytes (second element), the microglia is the true third element of the nervous centers, and in order to avoid confusion it should be separated in all descriptions from the macroglia or classical neuroglia with which it could be confused only in very defective preparations."

All the observations of del Rio-Hortega have been confirmed by numerous investigators. However, there are unclear points that follow, such as its differentiation from the oligodendroglia, its participation in the glia reticulum, its alliance with the reticulo-endothelial system, whether it is the predominant or entire source of the compound granular cells and whether its origin is ependymal or meningeal. The author gives his views on the subject:

1. The microglia is derived from the polyblasts or embryonal cells of the meninges during later stages of development and after birth, and it continues to penetrate the nerve tissue for a considerable period.

2. During this migration, rounded and ameboid forms are found, indicating mobility, but the cells later ramify and on reaching definitive location send out delicate tortuous branching processes with lateral spines which end freely without

anastomosing with each other or with the neuroglial elements. "The microglia lives in the neuroglia syncytium but does not take part in its formation. There are no transitions between microglia and oligodendroglia. . . .

3. "The microglia represents, in the nerve centers, the reticulo-endothelial system in its largest sense and possesses qualities so far known of fixing certain colloids and of phagocytizing red blood cells and cellular débris. Its physiologic rôle is concerned with the elimination of substances derived from the metabolism or from the destruction of nerve cells. . . .

4. "The microglia takes active part in all the inflammatory and necrotic processes of nerve tissue, and by its mobility and phagocytic power takes on elongated forms (rod cells) or becomes laminated and rounded (fat granule cells). The fat granule cells originate exclusively from the microglia and histiocytes."

Histogenesis and Cytogenesis of the Microglia.—The microglia becomes visible in the last period of embryonic development, when the meningeal and vascular organization of the brain is well developed. Thus, in the superficial white matter and in the depths of the hemispheres of new-born animals a large quantity of microglia is distributed unequally. It is heaped up next to the pia and follows the vessels even to the ependyma. There are two principal sources of microglia in the brain: the superior choroidal membrane and the pia covering the cerebral peduncles, lower down in the inferior choroidal membrane and in the spinal meninges. The large blood vessels give rise to small numbers. These microglia elements travel through the tissues and rapidly take up their station at a distance from their origin. It is not known exactly what elements give rise to the microglia, but it would seem to be the polyblasts in the pia. These can develop into macrophages, fibroblasts, endothelial cells, etc., the polyblasts being fundamental. There is no proof that these cells arise from the mononuclears of the blood.

The presence of these rather youthful cells, rounded, with spongy, vacuolated cytoplasm containing little drops of fat, has been noted frequently and has been mistaken for an inflammatory reaction (encephalitis interstitialis neonatorum); this is a normal observation, however.

The cells can be traced from their origin by their selective reaction toward the silver carbonate stain. The migration of these cells takes place rapidly, and in the later stages they orient themselves in regard to the tissue in which they exist. The ameboid forms disappear progressively as myelinization continues.

Morphology of the Resting Microglia.—With aniline stains the microglia nuclei are polymorphic, rounded, elongated, triangular, etc., and sometimes curved singly or doubly. The chromatin content is almost identical with that of lymphocytes, that is, a large number of granules with a large nucleolus. The astrocytes, on the other hand, have round nuclei with delicate chromatin granules and small nucleoli. The oligodendrocytes have spherical nuclei rich in chromatin.

The cytoplasm of the microglia has an affinity for colloidal silver. Otherwise, the processes could not be seen. From the perinuclear mass there are two, three or many processes varying in size, ramifications and length, and they have many secondary and tertiary branches and delicate spines. The termination of these processes is free. The protoplasm is more or less spongy at the origin of these processes and the edges are often stained intensely, but no Golgi apparatus, specific granulations or mitochondria have been found. Nevertheless, the centrosome is found next to the nucleus. Cellular inclusions are common, and often argentophilic.

Among the varieties there are unipolar, bipolar, multipolar and laminated forms. The variety is the expression of the plasticity of the protoplasm and indicates the varied forms of tissue tension.

The microglia elements penetrate individually into the nerve tissue and always preserve their individuality. Cell division is usually by amitosis during immigration from the meninges, and by karyokinesis during phagocytosis in pathologic cases. Therefore, amitoses are sometimes found, but rather infrequently. On account of this cellular individuality, the microglia can react very early in pathologic cases and gather in huge numbers in damaged areas.

Distribution and Connections of the Microglia.—The microglia is present in all divisions and in all parts of the nervous system. In the gray matter it is distributed fairly regularly, yet the processes seldom connect and never form a plexus.

There are fairly numerous cells of multipolar type in the superficial layer of the cortex, but most of the cells are located in the pyramidal layers. There are minor differences in the various parts of the brain.

The cerebellar cortex is likewise strewn with microgliocytes, following the dendrites of the Purkinje cells, and they are more numerous in the granule layer.

In the bulb and cord the microglia has no special characteristics. Although these cells are scattered through the nerve substance, there are many close to the vessels. They cluster to some extent around the nerve cells and are apt to be confused with the oligodendroglia. In the white matter they are often found along the course of the capillaries and small vessels. The cells can be found flattened out against the adventitia along the vessel.

Morphology of Active Microglia.—During the immigration into the nerve tissues, the microglia undergoes a complete morphologic evolution, passing by means of the emission of processes from the round forms to complicated stellate forms. In pathologic processes these elements undergo retrograde metamorphosis; therefore, the "plasticity and ameboidism" of these cells should be recognized.

The function of phagocytosis is accompanied by the extension and retraction of short pseudopodia. "When the microglia becomes active following an injury to nervous tissue, first those elements nearest the part, and, almost immediately, others situated at a distance travel through the feltwork, thanks to ameboid and stereotropic phenomena; thirdly, the increase of microglia is brought about by proliferation of the hypertrophied globular elements." Experiments upon the newborn cat, whose cortex is almost devoid of microglia, shows that an injury is followed by rapid migration of microglia from the white matter. In parts destroyed and softened by burning, the microglia undertakes its cleaning-up function and shows typical characteristics of phagocytes in action. Its processes are short or absent. Pseudopods develop, the cell takes on a rounded form with ameboid movements and contains granules. Erythrocytes, and even polynuclear leukocytes may be phagocytized.

The first appreciable change in the cells is an increase in the volume — first of the dendrites, then of the cytoplasm. The flexibility and delicacy of the processes disappear; the processes have a shortened, angulated contour, equipped with spines; sometimes they become nodular. In the second place the dendrites become shortened, the cytoplasm swells and becomes reticulated.

In developing, the nucleus becomes more elongated and the processes heavy, and the cell has a tendency to assume a vertical position, with its processes spreading along those of the pyramidal cells. Thus the rod cells are formed.

Laminated forms are found in all inflammatory conditions, forming sheaths, as it were, of the nerve cells, and even of the small vessels.

In phagocytosis these cells become swollen, the processes are lost, and the compound granule cells form.

The microglia belongs to the reticulo-endothelial system, but it would seem to be somewhat specialized, as are those minor reticulo-endothelial systems of the liver and lymph-nodes. The most striking difference is the inability to impregnate these cells by colloidal substance; yet this is due to the hematoencephalic barrier formed by the glia fibrils.

When the barrier is broken or when cultures of microglia are examined, the fixation of colloidal particles is easily observed. The scavenger cells are made up entirely of microglia. Neither macroglia nor oligodendroglia takes part in this phagocytosis.

Within the substance of these cells materials undergo transformation into lipoid, fat, iron, etc., and one finds amorphous granules which have not yet been elaborated. These cells transport the material to the perivascular spaces. "Although lipoid granules have been seen in the macroglia and oligodendroglia, it

is generally held that they are degenerative phenomena of the protoplasm. Nevertheless, certain authors believe that phagocytic function is participated in by the macroglia."

General Function of the Microglia.—The activity of the microglia varies in different cases of nervous disease; it is active in traumatic, inflammatory and necrotic lesions, and inactive in compression and intoxication. There is no primary proliferation of the microglia.

Traumatic Lesions: All traumatisms associated with destruction of nerve tissue are followed by mobilization of the microglia in and about the lesion. This is already recognizable in twelve hours by the swollen, retracted processes, and in twenty-four hours ameboid forms are actively phagocytic. The materials taken in are elaborated and digested so that fatty granule cells are formed, but only after from four to six days can hemosiderin be recognized. Thus, destroyed materials are removed, and shortly afterward, while the microglia still fills the cavity, the cicatricial gliosis begins to be formed. Nevertheless, the phagocytic cells may be recognized for two or three months, even in small lesions. Nuclear stains indicate cell division by mitosis in and about the affected area.

Necrobiosis: The microglia is very active in vascular occlusion, both those cells actually in the necrotic area and those adjacent to it combining to make a very large collection. The detritus is phagocytized and the process of regeneration goes forward. Later on, the cicatrizing reaction of the neuroglia begins, as well as new formation of vessels and of connective tissue and even slight initiation of nerve fibers. Even in old lesions the pigmented and fatty cells can be found. Formerly observers were surprised to find leukocytic elements in the necrotic areas very early, but special stains indicate that these are of microglial origin. The small necrobiotic areas, the senile plaques, are participated in by the microglia. Following an unknown process, which provokes swelling of the axon, with bursting and scattering, rosets are formed and the microglia begins its phagocytic activity. Gliosis follows it.

Acute Inflammation: The microglia is very active in acute inflammatory processes, becomes phagocytic even at some distance from the site of the lesion, and tends especially to be gathered about the vessels.

Chronic Inflammation: The microglia increases slowly in such conditions and is characterized more particularly by growth in size of both the nucleus and the processes, so that gigantic forms containing argentophilic lipoid and iron granules are formed. They are particularly characteristic in dementia paralytica, but are much more numerous in certain cases of syphilitic oligophrenia. In rabies and other subacute infections there is a moderate increase in both the size and the number of these cells, and particularly in rabies the laminated clinging to nerve cells and vessels is outstanding.

Granulomatous Inflammation: The microglia plays a prominent rôle in gummas and tubercles, surrounding the primitive follicles and later the caseous areas. However, since such inflammations usually involve the mesoblastic elements, "it is excessively difficult in the inflamed parts to differentiate the active phagocytic microglia from the equally active histiocytes, since both these cells evolve toward fatty granule cells and form fusiform shapes with lipoid inclusions." Only at the periphery where the phenomena of infiltration and of destruction are less accentuated can the cells be distinguished.

Intoxications: The activity of the microglia is less in intoxications. It would seem that it resists chemical substances introduced through the blood stream, and even in such cases as lead poisoning there is no significant change.

Compression: The microglia does not react to compression. Only when circumscribed tumors provoke some destruction of the nerve tissue by pressure does the microglia become active.

Tumors: Infiltrating tumors of various types are associated with active microglia so that Penfield has spoken of gliomatophagy, but the microglia apparently gives rise to no tumor of its own.

THE MORPHOLOGIC IDENTITY OF THE MICROGLIA WITH OTHER HISTIOCYTIC ELEMENTS. FABIO VISINTINI.

Various studies have indicated that the microglia is a special modification derived from differentiation of mesoblastic elements. Its relation to the reticulo-endothelial system has been proved. The author therefore attempted with Bolsi's method to find identical cells in other organs. Morphologically, similar cells were found in the heart muscle, voluntary muscles and muscles of the bladder.

DISCUSSION

DR. ROUSSY: The resemblance noted by Visintini between the cells in the interstices of muscle fibers and the microglia do not allow him to state that they are identical. Although the phagocytic phenomena are specially evident in the microglia I believe that they can also be found in the macroglia.

DR. LORENTE: In cases of dementia paralytica, senile dementia, rabies, etc., that we have studied, we have found ameboid neuroglia cells together with the fibrillar alteration in the cells next to the ependyma and the well known alterations of the microglia. However, we have never found alterations in the neuroglia that made us believe in an active phagocytosis by the neuroglia.

DR. MIR: In animals in which the cortex is compressed by a paraffin tumor there is a barely perceptible proliferation of the neuroglia, and the microglia is not changed except when the cortex is damaged.

THE PATHOLOGIC REACTIONS OF THE NEUROGLIA. G. MARINESCO.

Neuroglia cells are polymorphous, and in pathologic states the contour becomes even more irregular. The multiplication is sometimes active, either by direct or by indirect division. The osmotic character is well shown by the fact that cells may swell to three times their diameter. Neuroglia has remarkable properties of tropism and polarity, particularly in relation to the vessels. The vascular foot or tube establishes a direct relationship between the vascular wall and the neuroglia cell. Just what the meaning of this is, is not certain.

The ameboid change cannot be considered as progressive, but it is entirely degenerative, probably owing to a change in the intracellular p_H and its osmotic tension. In degeneration the processes may break up without previous swelling, and the cell or its clasmatodendrosis may be preceded by swelling of both the cell body and the processes.

Microglia and oligodendroglia seem to exist side by side, as it were, in symbiosis. However, they react very differently to harmful agents. "The essential element of phagocytosis in the central nervous system is represented by ameboid microglia." However, in acute and subacute infections the polymorphonuclear leukocytes are also active. While the neuroglia plays no active phagocytic rôle, nevertheless it is concerned in the metabolism of iron, calcium and glycogen, and especially in amaurotic idiocy are there a number of glycogen granules in the glia cells.

TISSUE CULTURE OF NEUROGLIA AND MICROGLIA. G. MARINESCO and I. MINEA.

Small fragments of the brain from a cat a few weeks old are cultivated in the animal's own plasma. In two hours there are certain cells at the boundary between the cortex and white matter that are distinguished by their marked argentophilia. The processes are very granular. There is slight tumefaction of the glia cells in the cerebral cortex. The number of argentophilic neuroglia cells increases with it, and dendrolysis is progressive. Cytolysis likewise begins, and in six hours irregular "Füllkörperchen" are observed. In twenty-six hours, the neuroglia has almost completely disappeared, and in forty-eight hours the cells are practically no longer recognizable. Thus, the pathologic processes recognized in man are seen in tissue culture. Although the microglia is much more difficult to impregnate

in tissue culture, the processes seem extremely delicate and covered with fine granules. There seems, therefore, to be no progressive change in the neuroglia when the circulation is suppressed. The oligodendroglia likewise undergoes only degenerative changes.

DISCUSSION

DR. CHOROSCHKO: The introduction of nerve tissue into the organism is followed by changes in the nerve tissue. Under the influence of neurotoxins, the nerve cells alone degenerate while the neuroglia proliferates. There is little indication of anaphylaxis from the injection of nerve tissue.

MICROGLIA AND OLIGODENDROGLIA STUDIED BY SILVER METHODS AND VITAL STAINING. DINO BOLSI.

By a different method, Bolsi has demonstrated the phagocytic function of the microglia. However, the oligodendroglia does not take part in this phagocytosis. The adventitial cells of the blood vessel also take part in the formation of compound granule cells. The macroglia likewise is incapable of being transformed into compound granule cells, although through its hypertrophy and hyperplasia it has an important cicatrizing function. Blood pigment is never found in the macroglia or oligodendroglia. These opinions are borne out both by selective silver staining and by vital staining. The capacity of the microglia for fixing vital stains deeply assimilates it to the histiocytic system of Aschoff.

DISCUSSION

DR. ROUSSY: The conditions of study of the foregoing authors have not been identical with ours. They study processes of rapid evolution, while we use the more slowly progressive lesions. The photomicrographs illustrating our work show clearly that the astrocytes can contain granules in their interior.

DR. GOZZANO: In Schilder's encephalomyelopathy, compound granule cells are in close relationship to the foci of demyelinization. These cells are formed exclusively by the microglia, while the macroglia shows hypertrophy and hyperplasia with regression, but no transition forms occur between astrocytes and granular cells. Even later, in older lesions the macroglia and oligodendroglia never become granule cells.

VITAL STAINING OF THE MICROGLIA. MARIE PIOLTI.

The microglia is not stained by vital stains under normal conditions, not even in induced meningitis and other injuries, nor in chronic inflammations. This indicates the strength of the hemato-encephalic barrier. Piolti used lead to break down this barrier, as well as needle punctures, accompanied by injections of trypan blue. Even under these conditions the microglia is seldom observed to contain any granules except in the immediate vicinity of the injury.

NEUROGLIA OF THE NEUROHYPOPHYSIS. P. KISSEL.

Each capillary in the posterior lobe has a fine network of neuroglia fibers about it, as well as processes going down in small baskets or feet. Astrocytes are rather small, though some are large and irregular. One or two processes is the usual number. These processes are usually long and uniform in thickness. Droplets of colloid derived from the anterior lobe can be found in the perivascular spaces of the posterior lobe.

MUCOID DEGENERATION OF THE OLIGODENDROGLIA. PAUL PAGES.

Degeneration of the oligodendroglia gives rise to a substance that gives a cytochemical reaction for mucus. This seems to be associated with the disappearance of the oxydase reaction.

MODIFICATIONS OF THE GOLD SUBLIMATE METHOD FOR THE NEUROGLIA. DINU RAILEANU.

The essential modification is further treatment with bromide before impregnation. Greater selectivity is claimed.

ANOMALIES OF GLIA TISSUE. H. BRUNSCHWEILER.

Sections of the medulla of a microcephalic child showed several islands made up of very delicate fibers of glia tissue. There was marked malformation of the olive. In the embryo a delicate web of fibers exists in the region of the future olive, derived from the lateral extensions of the bulb. These islets, developing precociously, might prevent the proper migration of nerve cells and fibrous extensions. Such architectural defects might be the basis of certain hereditary and systemic diseases.

DISCUSSION

DR. AYALA: The microglia was the subject of numerous studies of earlier Italian anatomists. In regard to the gliomas, it seems doubtful whether the classification of Bailey and Cushing is practical at the present time, but one hesitates to keep on with the classic divisions of the gliomas made by Virchow and others.

ORIGIN OF THE MICROGLIA. M. GOZZANO.

Cytogenesis has not yet indicated the derivation of the microglia. Four possible origins are mentioned: ependymal, vascular, hemic, and meningochoroidal. The first is very improbable; the second has not yet been proved, and the third has been definitely disproved. The meningochoroidal origin is the most probable.

In vital staining one finds numerous histiocytes in the choroidal and meningeal structures in new-born animals. The color is practically exclusively in the choroidal structures, while the meninges are almost free from the dye. It would seem that the microglia is of histiocytic origin.

In insulin intoxication the microglia undergoes acute swelling and clasmatodendrosis. This may have given rise to confusion with the swollen oligodendroglia cells.

MICROGLIA IN THE NEUROTROPIC ECTODERMOSES. ALBERTO LORENTE.

In experimental animals inoculated with different strains of virus, fatty granule cells develop at the point of inoculation. Rod cells are found throughout the neuraxis. This is not a specific reaction. However, the greater the neurotropism the greater the tendency toward satellite formation.

POSSIBILITIES FOR FINER HISTOCHEMICAL STUDIES OF MENINGO-ENCEPHALIC GLIOSIS. CHARLES OBERLING.

Gliosis takes place particularly at the periphery of the nerve tissue and invades the meninges. Monster cells form a dense fibrillary meshwork. The ganglion cells are preserved. The cerebellum, the pons, the parietal region and the optic nerve have been observed in this disease, and in all cases there is tumor. The glioblastoma seems the most common, although it has occurred in cases of meningoblastoma.

CONCLUSIONS

DR. ROUSSY: On several occasions I have discussed the communications which were made on the nature of the microglia, believing that the discussion might thus be made more active and useful. If I have overstepped the extreme bounds, I beg our president's pardon.

First, I wish to thank our foreign colleagues, Italian and Spanish, for having brought us the results of their researches.

I must also sum up in a few words the principal elements of this debate, in the course of which opposite opinions have been enunciated concerning the nature of the microglia and the origin of the granule cells.

Our Italian colleagues throw themselves without reserve to the thesis held by del Rio-Hortega and his school, a thesis which has again been taken up in recent work by my eminent friend, Professor Marinesco, who considers the microglia of mesodermal origin.

With Lhermitte and Oberling, we believe, on the contrary — and our recent researches have confirmed this impression — that the arguments invoked in favor of the duality in origin and nature of the neuroglia do not bring conviction and that the classic theory of original unity of the neuroglia elements still holds.

Such a divergence of opinion rests on deductions drawn from observations of facts, and also, I trust, on the question of doctrine which is fundamental.

The differences of interpretation result, we have seen, from the methods employed (staining by aniline dyes and their derivatives or impregnation by metallic salts), which bring authors to consider the neuroglia as a vast syncytial tissue formed by elements individually very distinct. There are also different experimental procedures utilized which indicate that our results are not at all in accord with those of our Italian and Spanish colleagues as to the origin and nature of granule cells. We believe that all the elements of the neuroglia participate in their formation: the macroglia, the oligodendroglia and the microglia, although to different degrees according to the nature and duration of the destructive process which involves the nerve centers.

We believe, in short, that if the characters of stability and fixity of the astrocytes are predominant, these same elements can acquire, under given conditions, properties of mobilization and phagocytosis. But more time is necessary for them than for the microgliocytes and oligodendrocytes or histiocytes to be transformed into phagocytes. The illustrations of our report, the charts that are before us, show it clearly. I therefore ask our opponents to resume these experiments under the same conditions that we have instituted or to utilize an entirely different procedure which will permit them to study the phenomena of resorption of fatty substances and débris in the course of slow destructive processes. I should not be much surprised if they arrived at the same conclusions as we do.

I must repeat, in closing, what I said in the conclusions of our report, that all these divergences rest essentially on the question of embryologic doctrine: that of the specificity of the three layers of Remak, according to which the tissues preserve in the course of the evolution of individuals an absolute biologic specificity. The tissues of ectodermic or entodermic origin fulfil the functions of covering and of secretion and those of the highly differentiated systems, such as the nervous system. The mesodermal tissues have the functions of support, connection and nutrition.

Such a rigorous specificity brought to bear on the data secured by observation of invertebrates and of the lower vertebrates does not seem to be suitable for adaptation to the superior vertebrates, and especially to mammals. It is in contradiction to that which the study of the tissue reactions in the course of morbid processes teaches, and it shows clearly the biologic adaptation of tissues in the course of evolution. When the data of histophysiology are opposed to those of embryology, it is to the first, I believe, that preference should be given.

A study of neuroglia tissue admirably illustrates this idea. It shows that tissues of common embryologic nature and origin (nerve and glia tissue) can undergo strictly different adaptations. It shows also that the tissues of the organism termed "connective" — giving this word a physiologic sense — can rise from different layers: the first come from the mesoderm (especially the mesenchyma), and are the common connective tissues and their derivatives; the others from the ectoderm — the neuroglia. All the elements of these two tissues possess in high degree the great function of support, connection and nutrition which belong to connective tissue.

NEW YORK NEUROLOGICAL SOCIETY

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LOUIS CASAMAJOR, M.D., *President, in the Chair*

OXYCEPHALY AS A PATHOGENIC ENTITY. DR. ALEXANDER N. BRONFENBRENNER (by invitation).

Oxycephaly is treated as an expression of a compensatory process. A premature synostosis of the skull and intracranial hypertension (the latter being brought about by the inherent growth of the brain, demonstrable in the patients mainly by roentgen evidences of craniostenosis) are evaluated.

The process implies certain menace to the brain; therefore variations in the preserved functional capacity of the brain and in the degree of the deformity of the skull, as observed in separate instances of oxycephaly (and allied deformities of the skull), are interpreted as indicators: (1) of the efficiency of the compensatory readjustment and (2) of the degree to which the tissue of the brain has been involved by the factor responsible for the initiation of the premature synostosis; the greater the rate and vigor of synostosis and damage sustained by the tissue of the brain, the more apparent is amentia and the less outspoken is oxycephaly.

The ophthalmologic component of oxycephaly is looked on as a most frequent complication, but not as an indispensable phenomenon of the compensatory process. A differentiation between acrocephalosyndactylia and oxycephaly proper on an etiologic principle is advocated. Multiplicity of etiology is upheld as most probable. The author's cases indicate that tuberculosis and especially syphilis are probably underestimated as etiologic factors.

DISCUSSION

DR. H. H. TYSON (by invitation): As Dr. Bronfenbrenner informed me that he would not say much about optic canals in this condition, I shall refer to them. Oxycephaly is interesting to the ophthalmologist because of the changes in the orbit, the presence of exophthalmos, and the varying degrees of atrophy of the optic nerve which may be associated with the deformity of the skull in some cases.

Most authors agree that the deformity of the skull is due to premature synostosis of one or more cranial sutures, with a compensatory enlargement of the brain. There are many theories of the cause of the synostosis. Some authors consider rachitis as one of the principal causes; others have failed to find evidence to confirm that observation in their cases, and think that it is due to some other obscure underlying condition. Stokes thinks that an abnormal twist in the development of embryonal dysplasia is most probably the cause of the anomaly. F. A. Davis holds the opinion that it is due to some fault in development. Schüller (Vienna) considers that it is an anomaly of ossification; Patry reported a case in which the horizontal axis of the cornea was smaller than the vertical, which, being the reverse of the normal proportions, he considered as indicative of a congenital origin. Therefore, the consensus is that the deformity is probably due to a developmental defect.

The exophthalmos is due to the abnormal shallowness of the orbit, the average difference in depth from the normal being about 10 mm., and it is found in about 50 per cent of cases. The superciliary ridges are flattened, and in some cases there is a protrusion in the temporal regions with bending outward of the zygomatic arches. Some observers have found a narrowing of the optic canal in many cases of oxycephaly, while in other cases there was found an alternation in the position of the great wing of the sphenoid pushing forward the dorsum sellae turcicae so that it caused pressure on the optic nerves or chiasm.

The roentgenogram of the optic canal shows a cross-section which is distinctly triangular or pear-shaped, the apex of the triangle being directed downward and

outward. In oxycephaly, the length of the optic canal is usually much greater than normal, although its caliber is markedly contracted (Goalwin).

Nystagmus may also be present, and it is usually of the horizontal variety.

Optic atrophy is a common complication of the condition; often vision may be better than it would appear from the ophthalmoscopic appearance of the optic disks. Friedenwald thinks that the atrophy of the optic nerve is due to direct pressure exerted by the growing brain, owing to the synostosis of the sutures of the vault. Uhthoff is of the opinion that the intracranial pressure, with the destructive effects on the optic nerves and visual function, is due to the disproportionate size and consequent pressure exercised by the growing brain against the nonyielding cranium. I think that a careful roentgenologic examination of the optic canals in these patients will give another possible cause of the atrophy; one may find pressure being exerted on the optic nerves, either from an irregularity in the shape of the optic canal, or from a canal that is markedly contracted.

About three years ago, I examined the eyes of sixteen inmates of Letchworth Village who had deformed skulls, while Dr. Goalwin and Dr. Potter made roentgenologic examinations. The results were interesting; in fourteen cases, one canal was smaller than normal, in ten there was optic atrophy, and in eight the diameters of the optic canals were very small. In cases of oxycephaly with small foramina, optic disks indicative of optic atrophy were found, while in skulls with foramina of normal size the disks appeared normal. In one private case in which I was able to obtain an approximate visual field, I found that it corresponded with what would be expected from pressure at the location shown by the roentgenogram.

Two of the cases mentioned by Dr. Bronfenbrenner were included in those examined three years ago both ophthalmoscopically and roentgenologically. Mr. A. showed a marked contraction in one diameter of each optic canal, each being 2.6 mm. instead of about 4.3 mm., and the ophthalmoscope revealed optic atrophy. Mr. S. showed a right optic canal contracted in one diameter to 2.2 mm., while the diameter of the left optic canal was 3.9 mm. In this case the right optic disk showed atrophy of the optic nerve. It is interesting to note that in these cases, the eye with the poorest vision is usually the one with the most contracted optic canal. A normally functioning optic nerve has never been found in a canal with the size of less than 2.8 mm. in one diameter. The size of the largest diameter of the canal is apparently immaterial, as the smallest diameter seems to exert a preponderating influence on the nerve, irrespective of it. As a proof that the narrowing of the canal may have a deleterious effect on the optic nerve, there have been at least four cases in which operations for enlarging the optic canal have been performed, one by Schlosser and three by Hildebrand, who cut away the roof of the canal, with subsequent arrest of the optic atrophy and with improvement in vision. The number of cases examined roentgenologically and reported have been too few to be of great import, but while increased intracranial pressure, toxic and inflammatory disturbances may be primary or secondary causes, I am strongly of the opinion that in these cases the pressure exerted by the narrow optic canal, plus the stretching and kinking of the optic nerves, thus inducing a papillary stasis and optic neuritis with subsequent optic atrophy, is one of the chief causes of the lesion of the optic nerve and that it is associated with a developmental defect.

Dr. Daniel B. Kirby (by invitation): Dr. Tyson has covered the ophthalmologic phase completely. I saw the two patients of Dr. Bronfenbrenner. The colored boy had a large amount of myopia, and the elongation of the eyeball added to the appearance of exophthalmos. There may be a greater amount of exophthalmos in some cases of oxycephaly, and if it is extreme and accompanied by lagophthalmos one must consider protecting the cornea from exposure and ulceration. A plastic operation at the external canthus will protect the eye. Both these cases were in the stage of secondary atrophy of the optic nerve, and by looking at the fundi it would be difficult to say whether it was a postneuritic or a post-papilledematous atrophy. I do not know that one would recognize the cases as beginning oxycephaly if one saw the patients at the beginning of the condition.

One would probably attribute the papilledema to something else. Undoubtedly the patients have papilledema, and this can be explained by the increasing size of the brain in an inelastic skull. It is worth while to examine any papilledema with a binocular ophthalmoscope. One can often differentiate between a neuritis and a papilledema by observation with the binocular ophthalmoscope.

DR. HARRY A. GOALWIN (by invitation): I am glad to see so much interest exhibited in oxycephaly and in the deformed skull in general, because the condition occurs more frequently than is generally believed. In my first year of practice of cranial roentgenography, I saw sixteen patients with deformity of the skull with visual disturbances and eight patients with tumor of the optic nerve. It is fair to assume that the deformed skull is twice as frequent an occurrence as tumor of the optic nerve and therefore deserves a proportional amount of interest and information. The ophthalmologist is not the only one who should be interested in oxycephaly, because the clinical manifestations may resemble those of other diseases of the brain. The cases are frequently mistaken for tumor of the brain.

The typical deformity of oxycephaly is not merely increased height and intracranial pressure with premature closure of the coronal suture. The orbit is shallow and has an exaggerated slope of the roof and lateral wall. The slope of the normal orbital roof is about 30 degrees; in oxycephaly it may be 60 degrees or more. The lateral wall, normally sloping about 45 degrees toward the sagittal plane, may be parallel to the transverse plane. The sella turcica is usually deformed. When a roentgenogram of the sella turcica alone is taken, it is easy to make a mistaken diagnosis of pituitary tumor. This should be a warning to ophthalmologists and neurologists never to ask for "an x-ray of the sella turcica."

The cross-section of the normal optic canal is roughly that of a quadrant of a circle, the limiting radii forming the roof and mesial walls and the arc forming the floor and temporal wall. If one imagines a ring of this shape, made of soft rubber, fixed at the lower apex and pulled upward at the base, it is apparent that one would get a triangular figure. This is what happens in the oxycephalic skull. The optic canal is elongated in the direction which I have termed the "A" diameter and narrowed in the "B" diameter. In all cases of oxycephaly that I have seen, optic atrophy was present only when the canal was narrowed and always in proportion to such reduced measurement. This leads me to believe that, whatever may be the pathogenesis of the premature synostosis, the optic atrophy is produced by purely mechanical causes; beyond question it is one of the most important factors.

In addition to the change in shape and size of the cross-section, the optic canal also has a different profile and length. The arrested anteroposterior growth of the cranium not only is responsible for the increased slope of the orbital roof and lateral wall, but it produces a tilting backward of the roof of the optic canal, so that its posterior edge lies behind the floor, while in the normal skull it is anterior to the edge of the floor. The sulcus chiasmicus is also displaced backward. While the depth of the orbit is decreased, the distance from the sulcus chiasmicus to the posterior pole of the eyeball is increased, which results in tension on the optic nerve. There are therefore three mechanical factors in the production of optic atrophy in oxycephaly: (1) constriction of the optic canal, (2) elongation of the optic canal (it is from 5 to 10 mm. in length, while the normal is from 0 to 5 mm.), and (3) stretching of the optic nerve. To this must be added the increased intracranial pressure, which, however, is not so important as a direct factor, because the pressure on the fibers of the optic nerve is uniform, the fibers being bathed in a fluid of increased tension.

I was surprised to find patients with oxycephaly at Letchworth Village when I began the work there with Dr. Tyson. The teaching has been that these patients are above the average in intelligence. Professor Schüller, under whom I began this work, studied his cases in institutions for the blind, which accounts for his finding of the subjects to be bright. Naturally Dr. Bronfenbrenner's experience at an institution for the feebleminded is also biased.

DR. BYRON STOOKEY: Nothing has been said about the age at which oxycephaly occurs. It is present at birth, and many cases are uncovered in the first two or three years of life. Undoubtedly those cases in which associated deformities of the hand are noted give evidence that whatever the etiologic factor is, it is one of osteogenesis, as in cases showing syndactylism there must have been some disturbance in development as early as the seventh week of intrauterine life. Only recently, I saw a case at the Children's Hospital, and the suggestion was made that I try operative intervention. Any interference with a microcephalic skull is futile, because there is a neuro-defect; there has been a failure in development and the sutures have closed. However, in cases of oxycephaly there is a normally developing brain, with the sutures closing prematurely and preventing that development. Towne and Faber, in San Francisco, reported a case in which they had operated; the child was 2 years of age, and they cleaned the coronal suture on either side, and also carried the suture backward so as to produce three lines of suture; they reported that the patient was improved, and the picture shown two and a half years later seemed to present a normal-appearing child. The evidence that they were dealing with oxycephaly in the first place was not complete, but I know that the work of these men is thorough, and so I feel confident in accepting their diagnosis of oxycephaly. That is the only case of which I am aware in the literature. I have never performed an operation for this condition. It seems to me that it would be a possible procedure; it is generally conceded that synostosis takes place due to the displacement of the primary centers of ossification; that instead of being placed within the cranial bones, these primary centers come to lie against the coronal sutures on either side, and therefore ossification takes place with two adjacent centers close to each other. Therefore, a prompt and early union of these two sutures takes place, forming a solid mass, especially in the coronal sutures. If that is the accepted etiology, and it would seem to be the most likely one that is offered, as no etiologic factors are yet known, the condition being probably an atypical form of development, it is probable that an early operative procedure could be done in these cases, and that one could cut into the coronal suture and ream out an area and perhaps permit the skull to develop normally. I cannot conceive of any operation being of value in increasing the intracranial contents in older patients. It is obvious that there is an increased intracranial pressure. Here there is the absolute opposite of microcephaly because in that there is no increase in intracranial pressure, but a diminished intracranial pressure. The diagnosis is easy to make, and the indications are to give more room if it is possible. I believe that it would be worth while to operate early in some cases, by selecting them properly, and work out one or two operative procedures to see whether anything can be done.

DR. LOUIS CASAMAJOR: I have been much interested in this presentation and am glad to have an opportunity to look at the pictures and to hear the ophthalmologists. It is interesting that they seem to observe more cases than do the neurologists, because undoubtedly the primary symptom for which the patients consult a physician is visual difficulty.

I do not understand what Dr. Bronfenbrenner meant about the relation of syphilis and meningitis to this condition. It seems to me that the etiologic mechanism is probably not intracranial. The brain seems to develop rather well in spite of enormous handicaps, and the signs of pressure are probably due to the attempt of the brain to develop normally in a cranium that is abnormal and too small. In the pictures shown I was impressed by the fact that there is a definite change not only in the bones of the cranium, but in the extracranial bones. I do not see how the meninges, especially the leptomeninges, could bear any etiologic relationship to such a condition, but if the condition were dural, a pachymeningitis, one could conceive of changes in the bones of the skull due to a dural change, for the dura is the internal pericranium. However, that would not account for the changes in the orbit and the facial bones. From what I have seen, it seems to me to be an osseous anomaly, a point which Dr. Bronfenbrenner certainly made.

DR. A. BRONFENBRENNER: Dr. Casamajor wondered what I meant by saying that meningitis is apparently a link in the pathogenesis of oxycephaly. From Virchow's time it has been customary to discuss "meningitis" as the factor of a premature synostosis of the skull, though the term is hardly used in its etymologic meaning of an inflammation limited to either membrane of the brain. The point is that any pathologic process located intracranially, such as hemorrhage of the brain as the result of an injury at birth, encephalitis, gumma, etc., affects to a greater or less degree the meninges as well. Such a reactive condition of the membranes of the brain, through continuity, contiguity, impaired supply of blood, etc., may disturb the osteogenic balance in the calvarium and initiate a premature synostosis.

I hardly could present the ophthalmologic phase of oxycephaly as ably as it has been done by the participants in the discussion. The importance of changes in the eyes in oxycephaly has been substantiated by the discussion of roentgen observations in the orbits as most remarkable features of oxycephaly. For the sake of restoring the equilibrium amid all phases of the condition, I wish to say that the compensatory struggle to provide adequate room for the growing brain, notwithstanding the synostotic limitation of the adaptability of the skull, constitutes the essential phenomenon of the oxycephalic changes. This compensatory process implies a certain menace to the brain. Therefore, the instances of an insufficient compensation of the synostotic limitations in the adaptability of the skull will be found among the feebleminded, and will be identified by certain morphologic characteristics of undersized, malformed heads that under roentgen examination show evidences of craniostenosis.

TREATMENT FOR CEREBROSPINAL SYPHILIS WITH MALARIA: REPORT OF TWENTY-SIX CASES. DR. M. NEUSTAEDTER.

After reviewing the literature on the various theories of the specific action of malaria in neurosyphilis in contrast to the action of other nonspecific proteins, vaccines and fevers, the following report on the result of the malaria therapy in twenty-six cases was presented.

Twenty-three patients were treated in the Neurological Hospital, and three privately, between October, 1924, and November, 1927. After the conclusion of the malaria paroxysms, antisyphilitic therapy was continued.

The youngest patient was 20 and the oldest, 62 years of age; eleven patients (10 males and one female) had dementia paralytica; five (three males and two females), the tabetic form of dementia paralytica; one male, cerebrospinal syphilis, and nine (eight males and one female), tabes. The lungs, heart, kidneys and the general vascular system in all were in fairly good condition. Kirby and Gerstmann cautioned against the inoculation of malaria into excessively obese persons. Curiously, in case 17 of this series, a woman, aged 34, weighing more than 200 pounds (90.7 Kg.), not only stood eight paroxysms, with a temperature of 106 F. in some, as well as other patients, but showed the best result, with a complete remission so far, accomplishing her housework and social duties normally. Before treatment the tabetic patients were becoming progressively worse, and one had a perforating ulcer that has defied all medication for two years. All of them suffered from tabetic crises.

The malaria blood (tertian type) was obtained through the courtesy of Dr. Kirby from the Manhattan State Hospital; 4 cc. was injected intramuscularly and 1 cc. intravenously. The earliest chill appeared on the sixth day after inoculation, and the latest on the eighteenth; on the average it appeared on the ninth day. From five to twelve chills were allowed, depending on the condition of the patient, with eight as the average. All patients were considered weakened during the paroxysms, losing much weight, and it was found advantageous to support them with strychnine.

In seven patients the quotidian type of malaria developed, and in seventeen the tertian; one patient had no chills after two inoculations given at an interval of

two months, and one had only one chill. The plasmodium was found in only eighteen cases. The maximum temperature reached was 106.4 F. and the minimum, 102 F.

The blood picture showed a slight leukopenia after the series of chills in ten cases and a slight leukocytosis in two; in all others there was no appreciable variation after the paroxysms.

The Wassermann reaction of the blood became negative after six months, and remained negative for four years after treatment in only ten cases; it remained positive in six, and was unobtainable in ten patients because of comparatively early discharge from the hospital.

The Wassermann reaction of the spinal fluid became negative one year after treatment with malaria and combined antisyphilitic therapy in three cases, after two years in one case, after three years in two cases and after four years in three cases; it remained positive to the time of presentation in four cases, and was unobtainable in eight cases. In all cases the lymphocytosis was markedly reduced within a month after the culmination of the chills, but the albumin and globulin contents went parallel with the Wassermann reaction.

Improvement in the form of remission in patients with dementia paralytica was noted in seven cases; of these, three may be considered with full remission to date, the patients following their normal vocations; three patients were discharged improved both mentally and physically, but could not be traced; one remained unimproved, and was transferred to a state hospital, and three died, one after trauma.

The results of treatment in the five patients with the tabetic form of dementia paralytica were: In case 1, D. L., a bank clerk, improved mentally so that he was able to resume his vocation, and for six weeks he worked without making a single mistake. He was discharged, however, because he was too slow. After a year he began to relapse, and in spite of intensive antisyphilitic medication, he recently became maniacal and was transferred to a state hospital where he died of a hemorrhage of the brain. In case 16, W. S. improved mentally six months after inoculation with malaria and antisyphilitic medication, and is still under observation at the hospital, with a normal mentality. At the time of inoculation he had the already mentioned perforating ulcer on the sole of the left foot. This ulcer healed completely within three months after combined treatment with malaria and antisyphilitic therapy. In addition, both ankles were in the incipient stage of Charcot's joints. This remained quiescent for four years, but recently flared up and continued to become worse. In the remaining three cases, the patients were unimproved and were discharged at their own requests.

All of the nine tabetic patients improved physically, gaining from 10 to 20 pounds (4.5 to 9 Kg.). The crises were somewhat modified, but in none had they completely subsided. The tabetic process became stationary in seven cases. One patient died a year after treatment, and one remained unimproved. In case 18, in C. G., a carcinoma of the larynx developed a year previous to presentation, and the patient died.

The patient with cerebrospinal syphilis was discharged unimproved six months after treatment.

Summary and Conclusions.—Three cases, or about 11.5 per cent of the patients, died within a year after treatment. One patient improved, with a complete remission six months after the treatment, but suffered from a relapse a year later and died five years after the inoculation with malaria. Eighteen patients, about 69.2 per cent, were improved, and remained in good condition. Of the eleven patients with dementia paralytica, three, or 27.2 per cent, were following their vocations normally. Six patients, or about 23 per cent were unimproved.

These results practically coincide with those of other investigators.

DISCUSSION

Dr. Leland E. Hinsie: Dr. Neustaedter has given an excellent résumé of the theories pertaining to the mode of operation of malaria in cases of neuro-

syphilis. At the Psychiatric Institute we have been experimenting with malarial therapy for dementia paralytica since the early part of 1923. We feel that we cannot contribute anything of importance with respect to these particular ideas. It is probable, however, that we may later be able to add something through the use of a fever-producing machine known as the radiotherm which is now being employed in cases of dementia paralytica. By means of this apparatus a temperature of any desired height may be obtained. This is acquired through the influence of short radio waves. We hope to be able to reproduce the temperature curves as they are witnessed in cases in which the patients are treated with malaria. If this can be accomplished, we may be in a position to compare the clinical outcome in patients so treated with the clinical outcome in patients treated with malaria. A comparison of these results might assist in clearing up some of the theories that are now related to the rôle of plasmodium itself. At the present time our experiences are too meager to allow of any definite statement.

During the past few months, the members of the Institute staff have been assembling data on all the available cases in which patients with dementia paralytica were treated from 1923 to 1926. We have been fortunate in being able to reexamine 197 patients treated during that interval. They have been reexamined from the standpoint of degree of socialization, in addition to the mental, physical and laboratory status. All of the cases were of the neurosyphilitic order; moreover, almost all were diagnosed as dementia paralytica.

Of the 197 cases, the following brief summary, as of 1930, may be given. Some of the patients received malarial treatment alone, others received only treatment with tryparsamide, and a third group received combined treatment with malaria and tryparsamide. At present, 22 per cent of the 197 patients are in a stage of clinical remission; almost 18 per cent are improved; almost 20 per cent are unimproved, and 40 per cent are dead. In other words, 60 per cent of the patients are living. This is not a percentage to be expected in cases in which treatment was not given. Clinical remissions are present in 19 per cent of male patients treated with malaria, and in 30 per cent of female patients treated with malaria. We are not certain in the statement that with a lapse of years the rate of clinical remission rises in women patients and falls in men patients. The same tendency toward clinical remission and relatively the same ratio between men and women seem to obtain in patients treated by tryparsamide alone. The rate of remission among patients treated by combined therapy with malaria and tryparsamide is lower, namely, around 15 per cent. This may be explained in part, at least, because tryparsamide was commonly given after malaria had proved ineffective. As regards the response to treatment among males and females, it might be stated that for all the types of treatment indicated, the clinical remissions in 125 males were 18 per cent, and in 72 females 29 per cent. Furthermore, tryparsamide seems to enjoy a higher rate of remission than does malaria. We are reminded of the figures gathered from the literature by Bunker, who reported that of 542 patients treated with tryparsamide, full remission was recorded in 35 per cent, whereas, of 2,460 patients treated with malaria, full remission was recorded in 27 per cent.

As a result of our recent review we have noticed a particularly striking tendency for the laboratory observations in dementia paralytica to become completely negative. This refers to the Wassermann reactions of the blood and spinal fluid and the colloidal gold curve. There seems to be no definite correlation between laboratory observations and the clinical outcome. A patient in an excellent remission may show highly positive results in laboratory tests, whereas the tests may give negative results in a patient with advanced dementia.

DR. LEWIS D. STEVENSON: From experience at Bellevue, I have always believed that tryparsamide is a valuable and safe drug, if used in doses of not more than 2 Gm. At first we used doses of 3 Gm., and some cases of partial blindness and partial optic atrophy resulted. We have used some malaria therapy, but we have had remissions equally well with tryparsamide, and since tryparsamide

is so much safer, it seems to me that it is the treatment of choice in cases of dementia paralytica.

DR. M. NEUSTAEDTER: The main reason why I have never used tryparsamide is because I was afraid of atrophy of the optic nerve. The situation in the state institutions for the insane is different from that in a city hospital. The patient is committed and kept in the state institution. We cannot keep any patient in the city hospital. Patients even write letters to the commissioner if anything goes wrong, and we have to be careful. For that reason I do not care to risk an amblyopia, and have contented myself with malaria therapy.

Parallel with the treatment with malaria, I have also treated a series of ten patients with injections of milk. It is too early to report on the results.

Book Reviews

GESCHEHNIS UND ERLEBNIS. ZUGLEICH EINE HISTORIOLOGISCHE DEUTUNG DES PSYCHISCHENTRAUMAS UND DER RENTEN-NEUROSE. By ERWIN STRAUS. Price, 6.60 marks. Pp. 129. Berlin: Julius Springer, 1930.

"Occurrence and experience, a historiologic interpretation of the psychic trauma and compensation neurosis," takes up a problem very vital for psychopathology and for the whole psychodynamic conception.

German insurance and compensation laws and an unusually keenly disciplined system of obligatory written medical expert opinions in the cases of nervous sequelae of accidents have created the occasion and foundation for an extensive and intensive discussion of the compensation neurosis. In connection with this discussion, Erwin Straus, the editor of *Nervenarzt*, presents an interesting densely printed and densely knit analysis of the psychologic and logical principles involved. In contrast to some of the supererudite writing in these directions, Straus keeps fairly close to the specific issues involved in the "psychologic and pathopsychologic" inquiry into the relation of the happenings as such, and the experiences of the happenings and the senses in which the theorists and the practitioners in the field of traumatic neurosis use and fail to use essential distinctions. Unfortunately, he is still involved in much confusing complexity. His chief contention is with the elementalist in psychology, and especially the freudian use of the concept of psychic trauma, the pavlovian formulations and the problem or rôle of time in the theoretical discussions of this field. He takes issue with those who neglect the historical organization of man's thought of himself and who fail to recognize the necessity of surrendering the supremacy of sensation and perception in psychologic thinking (they cover only the happening but not the all important historical assignment or evaluation of the experience in and by the personality) and the necessity of a better consideration of memory and of the factors which make the difference between the individual reactions to accidents, and especially what makes an event appear as new and as potent and active in one's attitude to experience and to life. He aims to show that such a question as "When can we speak of disease in the traumatic neurosis?" cannot be settled within the field in question without determining whether the disease concept can apply in the same sense in somatic medicine, in the psychoses and in the neuroses. He is keenly concerned with the difference between conscientious theory and speculation and mere floundering with loose terms and Fragestellung, disregarding the peculiar problems and features of the subject with which one deals. He is obviously not satisfied with the uncritical and naive way in which psychology is treated and used, especially by those who biologize too easily and who fail to be clear on what they mean by neurosis or what some of us would call the differences between integrative levels. Unfortunately the booklet is written for the German supererudite and is difficult to digest without an attempt to translate it into plain thinking.

To give in detail the evolution of Straus' argument would call for a restatement and reformulation of the closely knit and yet discursive considerations. The enumeration of the chapters may give a taste of the type of discriminations he demands: 1. The representative function (the distinction between the person who went through a dangerous situation in narcosis or in full consciousness; or the sense in which one is justified in looking on specific experiences as the causal determiner of, let us say, a fetichism with inadequate consideration of the reason why one individual creates a fetichism and another digests the overspecific association). The reason why an incident affects different persons differently requires a study in the light of the topic of 2. The "historical modality," and the sense of familiarity and of novelty. Instinct as such has no historical

problems; but reference of a development to the antecedents must give due consideration to the characteristically historical organization of the personality. Straus gives an interesting discussion of the nature of the miser and the logical status of the analytic identification of money and feces, and especially also the question of what gives an experience the character of novelty and irrevocability, e. g., why the miser prefers the money with the sense of unlimited possibility while he cannot rise to contentment with any concrete use of the money. Straus thus comes to a critique of the genetic theories, one might say the too naively elementalistic psychologies, as discussed with regard to Freud's theory of anxiety (the excessive emphasis of the birth situation), and the difficulties with the Weber-Fechner law and the gnostic and pathic features of sensation (Foerster), then Pavlov's use of the "signal" in the attempt to build up a psychology out of the conditioned reflexes, adequate consideration of the internal setting and the sample facts specific to psychobiologic functioning, and Jung's idea of the collective unconscious, and the differences between the choice from real love and choice with mere sophistication. 3. The "thematic content." It is that which makes the specificity of the individual reactivity, evidently the recognition of something equivalent to what the Gestalt psychology wants to see recognized; something that calls for the distinction between happening and genuine full fledged personal experiencing (exemplified by a discussion of the different reactions to a fire on a stage).

This succession of chapters lays the foundation for a concept which he calls "deformation." The word presupposes the preexistence of something "formed." One deals here with the same issue which forces itself on the conscientious observer in present-day growth of the concept of integration, "holism", Gestalt, emergence, etc.—the need of correcting the shortcomings of elementalism. In contrast to Freud, who identifies the perversions with the original flounderings of the infant, Straus would want to limit sadism to a degradation of a necessarily more complex entity or level of development. Similarly he sees a "deformation" in the compensation neurotic who does not recover after the settlement of the case. Granting that some of these patients really were not pure victims of the craving for compensation, but wrongly diagnosed as that kind of pure Rentenneurosen, there are evidently some persons who continue to remain beneath the level of their capacity and opportunities, who remain in a rut and fail to make their grade again. It would seem better to use the term degradation, indicating the falling below a previously attained grade, i. e., something more definite than "form." There still remains the chance for possible confusion in the fact that one should not include in this concept the grade expected by others, but really the grade previously attained by the individual himself.

The booklet is a severe test of endurance of the level of attention to the highly complex standard of inclusiveness of critical erudition, no doubt maintained under the system of rigid academic competition and respect for the real attainment of the best attainable work (rather than good-enough success) so characteristic of the German intellectual morale. In contrast to some other products of superintellectual self-indulgences, this book is, however, much clearer and more pointed than even the same writer's book on "Suggestion" and so many of the metamedical and metapsychologic productions of the day. Nevertheless, one wishes that the presentation might be subjected to a restatement by the author with as much attention to a reading public as to his own rich flow of argumentation.

It may be that when our national bill for compensation cases shall exceed the annual budget of a billion dollars, there may develop a necessity for a real interest in the big problem of exploitation of the State under the heading of pensions and compensations to invalids, their relatives and their representatives in the political game. In Europe, where economic pressure affects the State and the individual alike, the compensation problem is much more acutely felt. The idea that discussions of the type of this one of Straus may claim an influence even in the practical and legislative spheres abroad might well make us conscious of our tremendous tendency to make a virtue of avoiding preoccupation with complex topics, and of condoning the aloofness of academic interest and rigorous

thinking from what happens in legislation supposed to protect the real victims of industry and war. Has medicine, and particularly neuropsychiatry, taken any active share in the recent pension and compensation legislation in the interest of the war veterans? What is our status as compared to the serious practical and theoretical efforts of our European confrères? Are we not missing an opportunity for valuable stimulation and service?

In these days of liberal reference to "psychic trauma" and psychic causes, a careful study of the psychic aspect of trauma in accidents is certainly of interest. What would be the manner of approach to such a topic on the part of our practical-minded workers? Why do we not feel the urge of closer study of what we mean by psychic trauma?

The German discussions are too involved. When shall our own rise above too ready acceptance of the expediency of passing by an important part of social and legal medicine? Straus' discussion might, however, prove stimulating to any one seriously interested in the research aspects of psychology and its formulations with psychopathology.

There is a valuable theoretical aspect to the topic. How could we work on what Straus suggests by his title?

There evidently is a distinction between a human organism going through a situation asleep and going through it awake, indifferent and definitely involved. There must be a wide difference in the many different degrees and types of involvement. One might be able to study the type without associative material and bring to a test the types in which unconscious trends might have to be stipulated or in which primary inattention is later transformed into haunting or profitable preoccupations. One might bring to various tests the unconscious and the subconscious and the co-conscious and the various ways in which experience is carried and is passively or actively potent. One would like to see not only a dialectic but a genuinely experiential if not actually experimental study. The World War offered some opportunities to secure a freer conception of the determination and nature of hysterogenous material supplementing the over-standardized Freudian "mechanisms." There is much work needed on psychogenic determination, and the traumatic neuroses and insurance neuroses should offer excellent material.

ÉTUDES SUR LES MALADIES FAMILIALES NERVEUSES ET DYSTROPHIQUES. By O. CROUZON. Price, 55 francs. Pp. 385. Paris: Masson & Cie, 1929.

This monograph gives a complete discussion of the familial nervous diseases. Crouzon classifies the latter into: (1) typical and (2) atypical familial maladies. The typical maladies are classified as follows:

1. Familial diseases in which the lesions are predominantly encephalic: (*a*) familial mental diseases — la folie héréditaire, insanity in twins, hereditary suicide, familial psychoses, familial dementias, etc.; (*b*) amaurotic idiocy; (*c*) Wilson's disease; (*d*) infantile cerebral diplegia; (*e*) cerebellar atrophy; (*f*) cerebellar hereditary ataxia.
2. Familial diseases in which the lesions are predominantly spinal: (*a*) Friedreich's disease; (*b*) spasmodic paraplegia (Strümpell-Lorraine); (*c*) amyotrophy of Charcot-Marie.
3. Familial hypertrophic neuritides.
4. Muscular diseases: (*a*) myopathies; (*b*) Thomsen's disease; (*c*) myatonia atrophica; (*d*) periodic paralysis.
5. Choreas, myoclonias and tremors.
6. Familial trophic disturbances: edema, neurofibromatosis, adiposity.
7. Familial neuro-ocular diseases.
8. Familial diseases of the endocrine glands.
9. Rare familial diseases of the nervous system.

The atypical familial diseases are classified as follows:

1. Spastic spinal paralysis with disturbances in vision (Jendrassik).

2. Spastic spinal paralysis with disturbances in speech, weakness of the eye muscles and nystagmus (Dreschfeld, Pelizaeus, Hodemaker, Bernhardt, et al.).
3. Spastic spinal paralysis with tremor and atrophy of the optic nerves (Freud).
4. Spastic spinal paralysis with idiocy (Homan, Bouchard, Pribam).
5. Spastic spinal paralysis with incoordination (Menzel, Nonne, Haushalter).
6. Myoclonus and optic atrophy.
7. Friedreich's disease and idiocy (Pritzsche).
8. Friedreich's disease with dystrophy.
9. Spinocerebellar hereditary ataxia with dystrophy.
10. Neuritic muscular atrophy with idiocy, amaurosis and bulbar disturbances (Bertolotti).
11. Spastic spinal paralysis with muscular dystrophy, nystagmus and tremor.
12. Dystrophy with pseudonystagmus.
13. Dystrophy with hypertonia, tremor, disturbances of speech and weakness of vision.
14. Ocular paralysis with loss of the patellar reflexes.
15. Nystagmus, intention tremor, cerebellar ataxia, spastic phenomena, contracture and arteriosclerosis (Kollarits).
16. Nystagmus, ataxia, bradylalia and spastic paralysis of the lower extremities (Merzbacher).
17. Optic atrophy, ocular paralysis and loss of the ocular reflexes (Kollarits).
18. Microcephaly, disturbances in intelligence, loss of the ocular reflexes with Babinski sign and dystrophy of the muscles and bones (Kollarits).
19. Imbecility, achondroplasia and scolioses.
20. Periodic family paralysis with dystrophy (Bernhardt).
21. Friedreich's disease with Huntington's chorea.
22. Dystrophy, idiocy, paralysis of the eye muscles and optic atrophy (Bac).
23. Idiocy, optic atrophy, spastic phenomena and epilepsy (Pesker).
24. Familial cerebellar atrophy.

Crouzon uses the term infantile encephalopathy, introduced by Brissaud, to include all forms of infantile encephalitis or infantile cerebral paralysis. He divides this group into several subgroups, depending on whether they are purely infantile or only sometimes infantile or familial. Under the cerebral diplegias Crouzon describes some cases of a familial disease with the clinical form of multiple sclerosis. This occurs in members of the same family and has been described by Pesker, and by Cestan and Guillain. The former found a complete arrest of the fibers of the entire neuraxis.

Crouzon reports a case in association with Souques and Bertrand of parkinsonism followed by a torsion spasm. Necropsy showed a lenticular degeneration, a degeneration of the pallidum and slight involvement of the thalamus.

The book includes excellent discussions of Friedreich's ataxia, cerebellar hereditary ataxia, craniofacial dysostosis and myoclonic epilepsy. The volume is extremely useful and can be freely recommended to neurologists.

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CONTENTS